Analysis and Visualization of Biological Networks

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Resource for Biocomputing, Visualization, and Informatics,
UCSF

Caveats

- Research in biological network analysis requires…
  - in-depth knowledge of graph theory
    - Which I'm not sure I have…
  - strong background in statistics
    - Which I know I don't have…
  - strong background in biology
    - Which I *think* I have…
- I'm not going to talk about cutting edge research
- I'm going to introduce some of the approaches and tools only

So, why am I here?

- Executive Director: NIH Resource for Biocomputing, Visualization, and Informatics
- 19 Years of Pharmaceutical Experience (Genentech)
- Cytoscape core team (4 years)
- Author:
  - Cytoscape layout mechanism
  - Cytoscape group mechanism
  - Metanode Plugin
  - clusterMaker
  - chemViz
  - structureViz

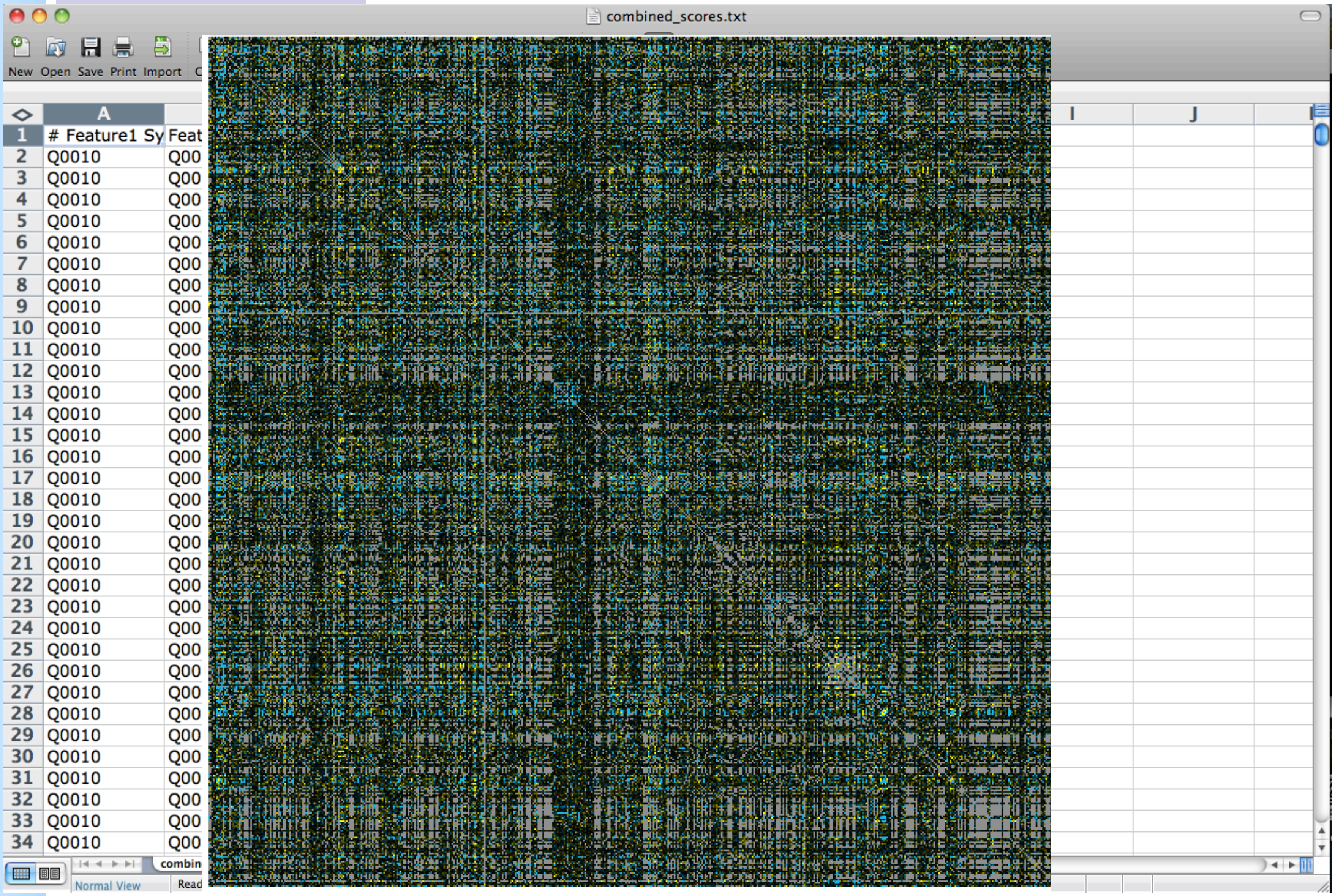
Why are you here?

- Bench biologists?
- Geneticists?
- Bioinformaticists?
- Mathematians?
- Cheminformaticians?
- Structural biologists?

Outline

- The Challenge
- Biological network taxonomy
- Analytical approaches
- Visualisation approaches
  - Data mapping
  - Layouts
- Tools
  - Cytoscape

The Challenge



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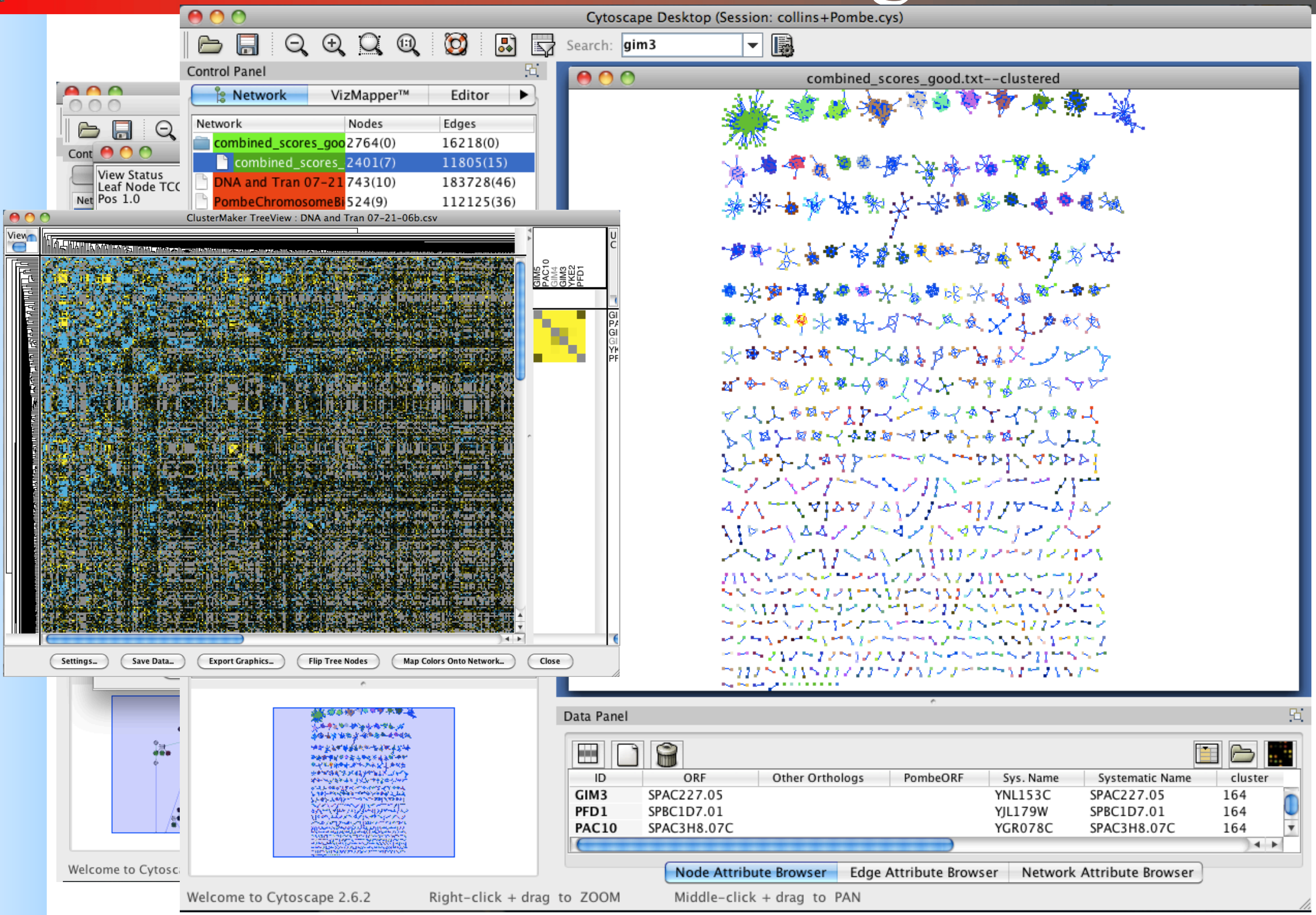
32	Q0010	Q00
33	Q0010	Q00
34	Q0010	Q00

The Challenge

- Biological networks (nodes and edges)
  - Seldom tell us anything by themselves
  - Analysis involves:
    - Understanding the characteristics of the network
      - Modularity
      - Comparison with other networks (specifically random networks)
  - Visualization involves:
    - Placing nodes in a meaningful way (layouts)
    - Mapping biologically relevant data to the network
      - Node size
      - Node color
      - Edge weights

The Challenge



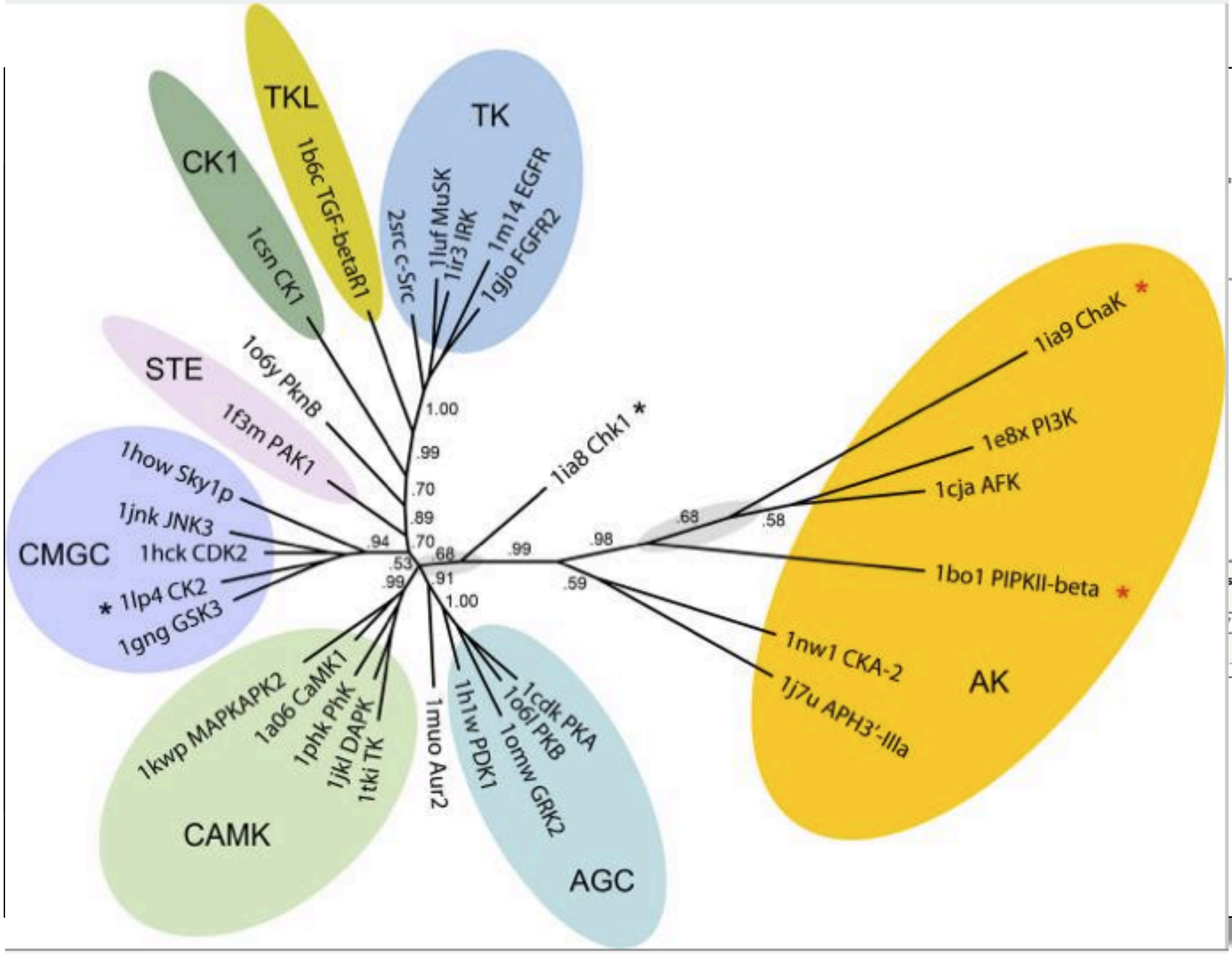
Search: gim3

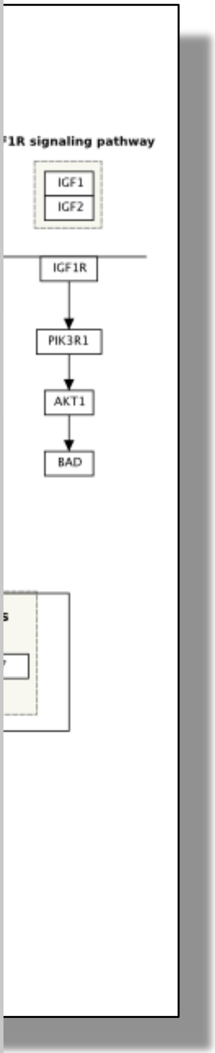
Network	Nodes	Edges
combined_scores_goo	2764(0)	16218(0)
combined_scores_	2401(7)	11805(15)
DNA and Tran 07-21	743(10)	183728(46)
PombeChromosomeBi	524(9)	112125(36)

ID	ORF	Other Orthologs	PombeORF	Sys. Name	Systematic Name	cluster
GIM3	SPAC227.05			YNL153C	SPAC227.05	164
PFD1	SPBC1D7.01			YJL179W	SPBC1D7.01	164
PAC10	SPAC3H8.07C			YGR078C	SPAC3H8.07C	164

Welcome to Cytoscape 2.6.2 Right-click + drag to ZOOM Middle-click + drag to PAN

Biological Network Taxonomy





Biological Network Taxonomy

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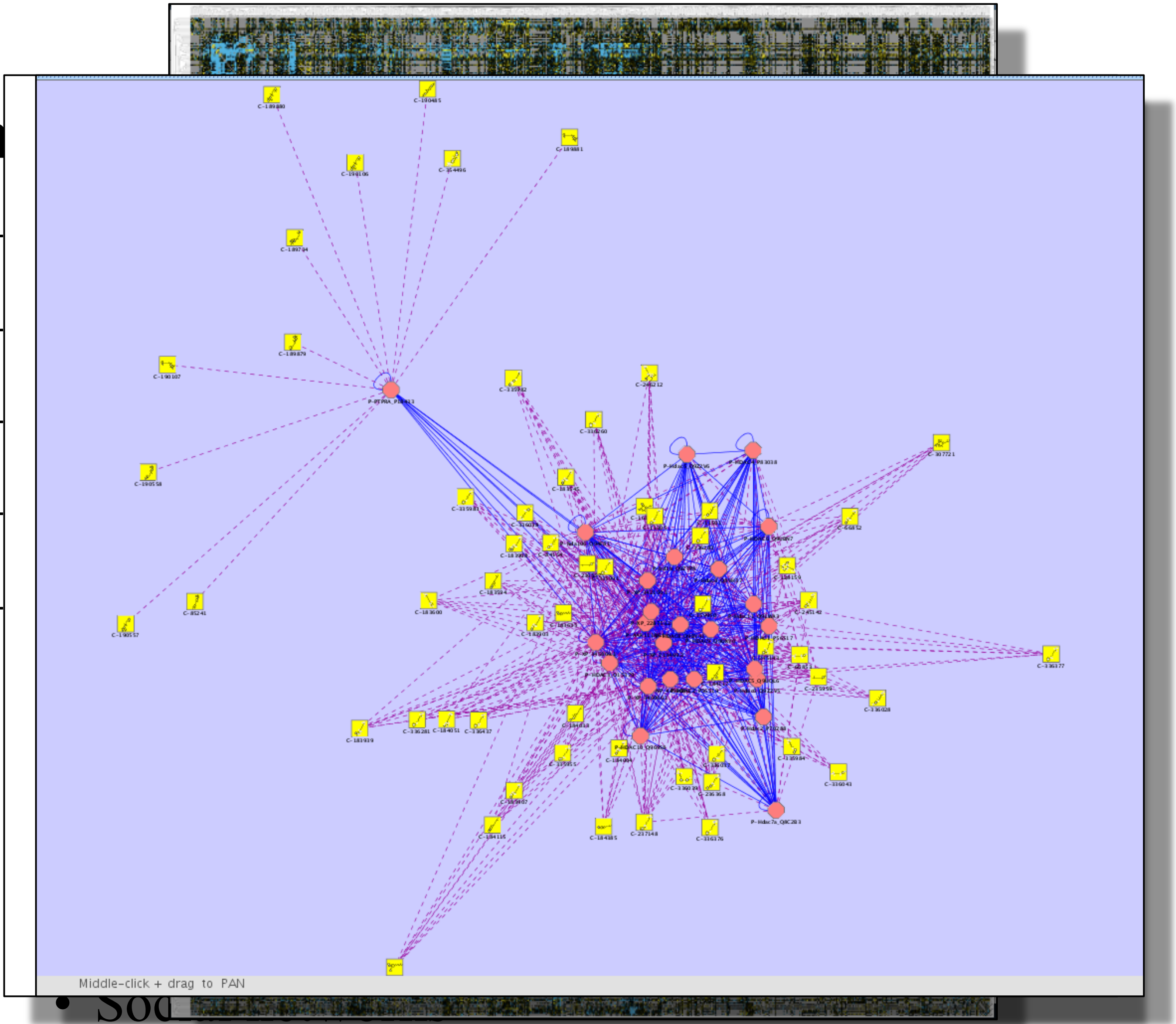

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Biological Network Taxonomy

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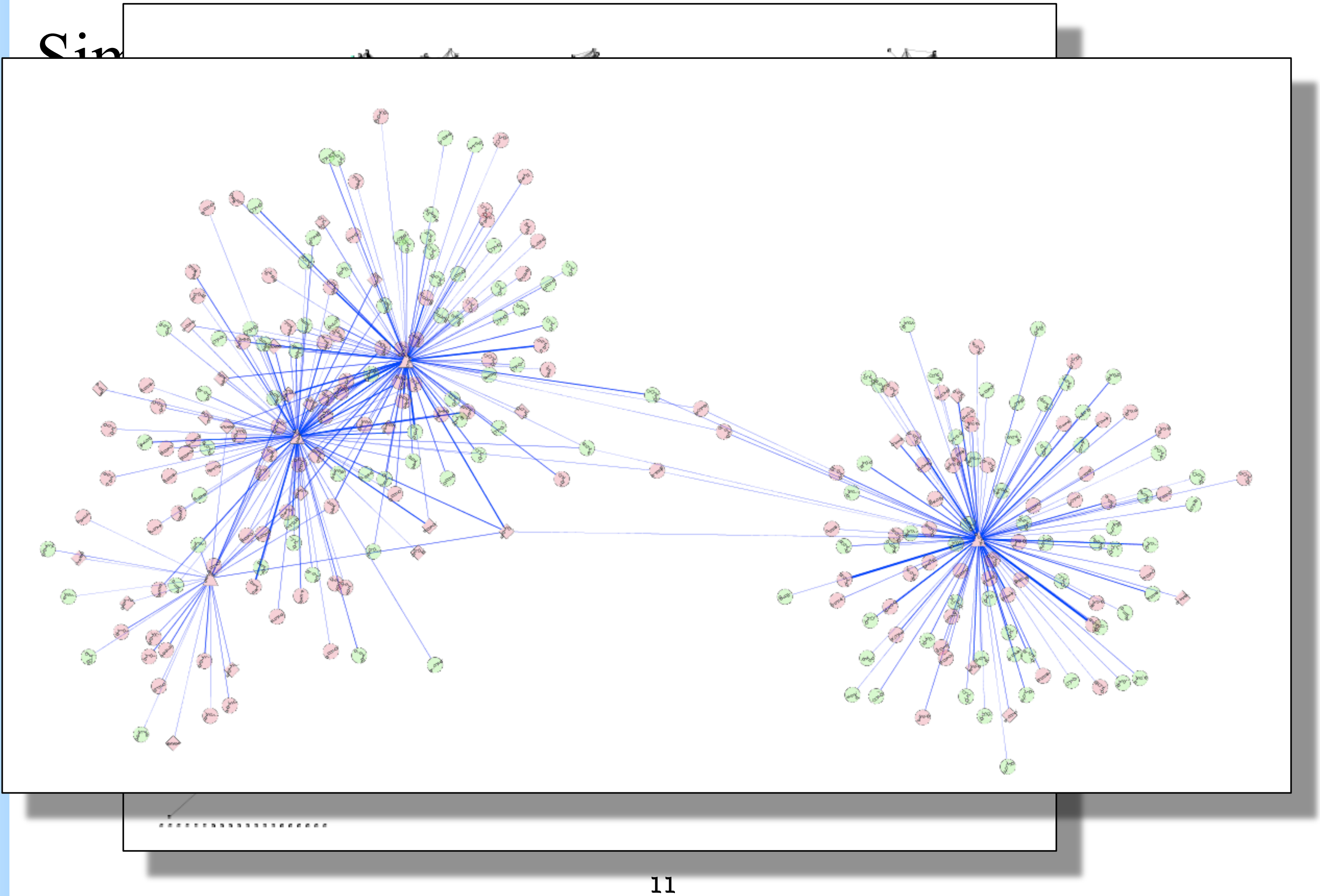

Analytical approaches

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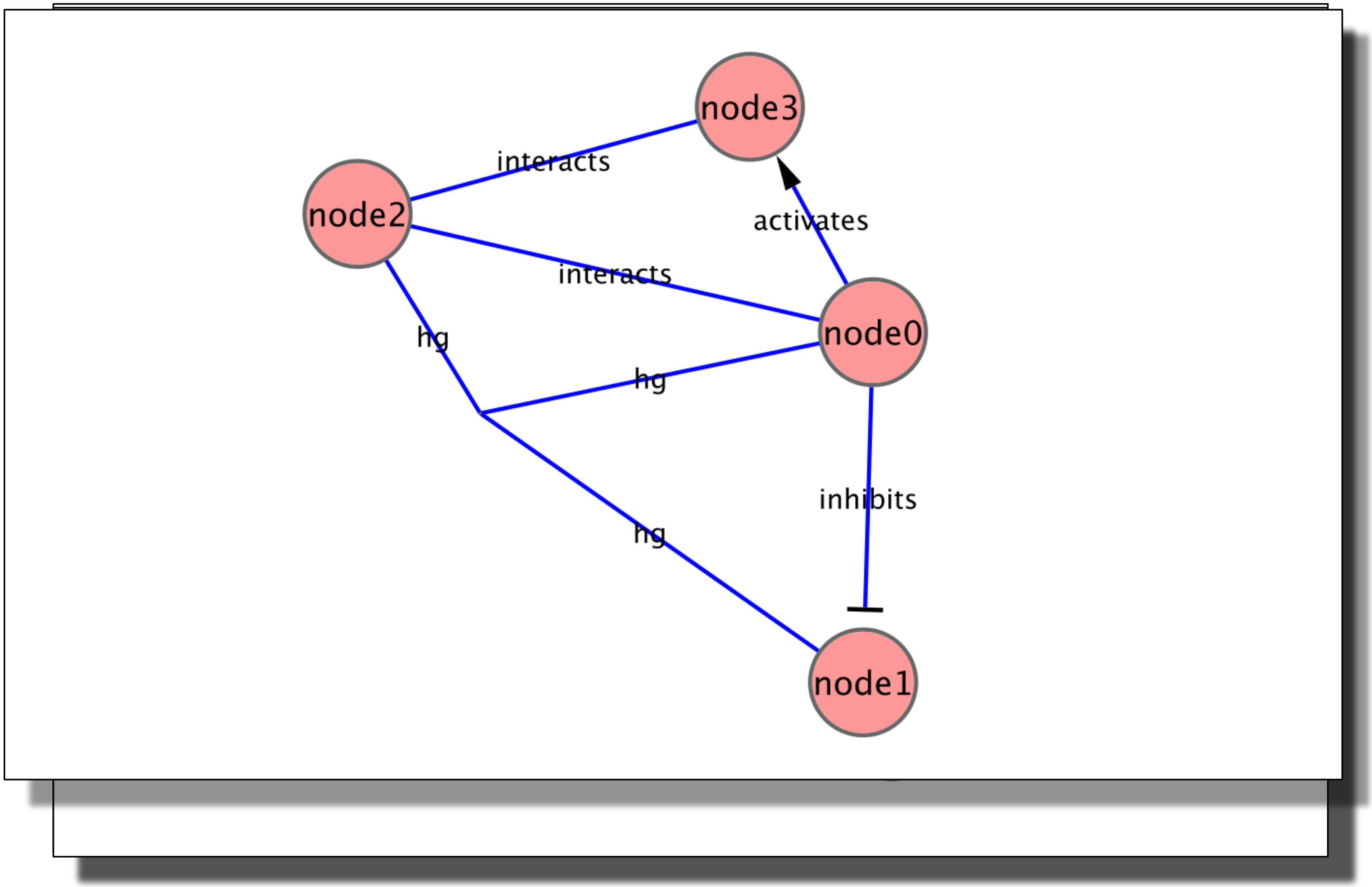
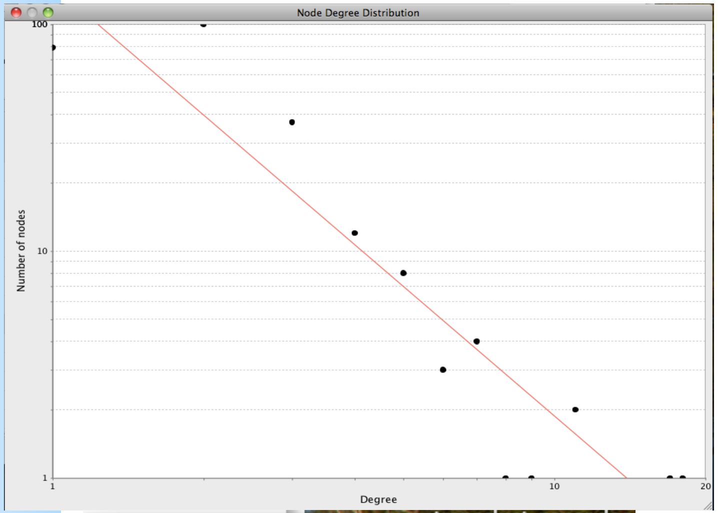
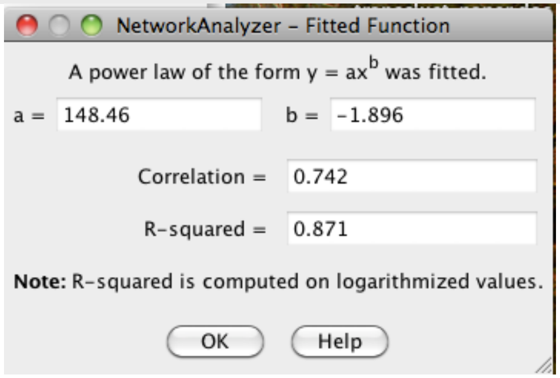


Analytical approaches

- Scale-free networks
  - Degree distribution follows power law: $P(k) \sim k^{-\gamma}$, where γ is a constant.
  - Result is that there are distinctive "hubs" (essential proteins?)
  - Overall, though, network is resilient to perturbation
  - Biological (and social) networks tend to be scale-free

Analytical approaches





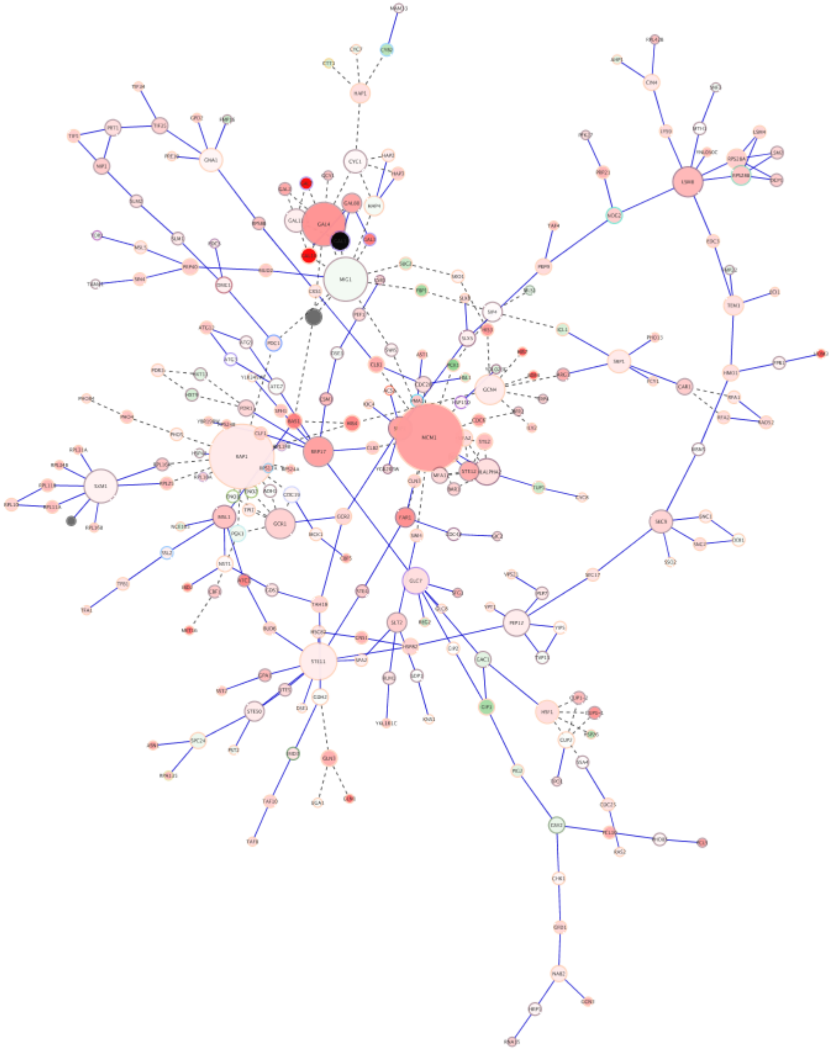
A power law of the form $y = ax^b$ was fitted.

a = 148.46 b = -1.896

Correlation = 0.742

R-squared = 0.871

Note: R-squared is computed on logarithmized values.



Analytical approaches

- Hierarchical networks

Analytical approaches

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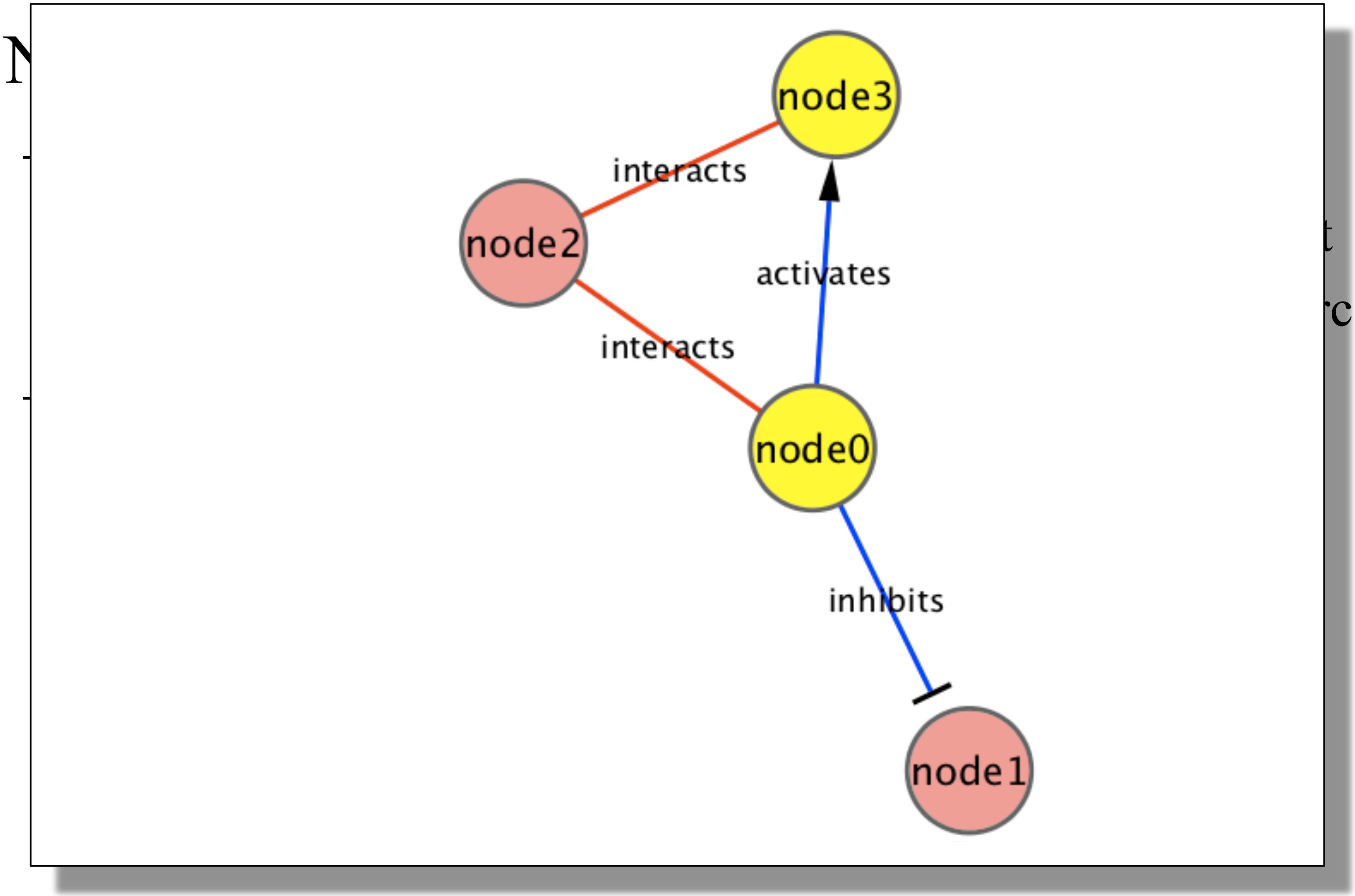

Analytical approaches

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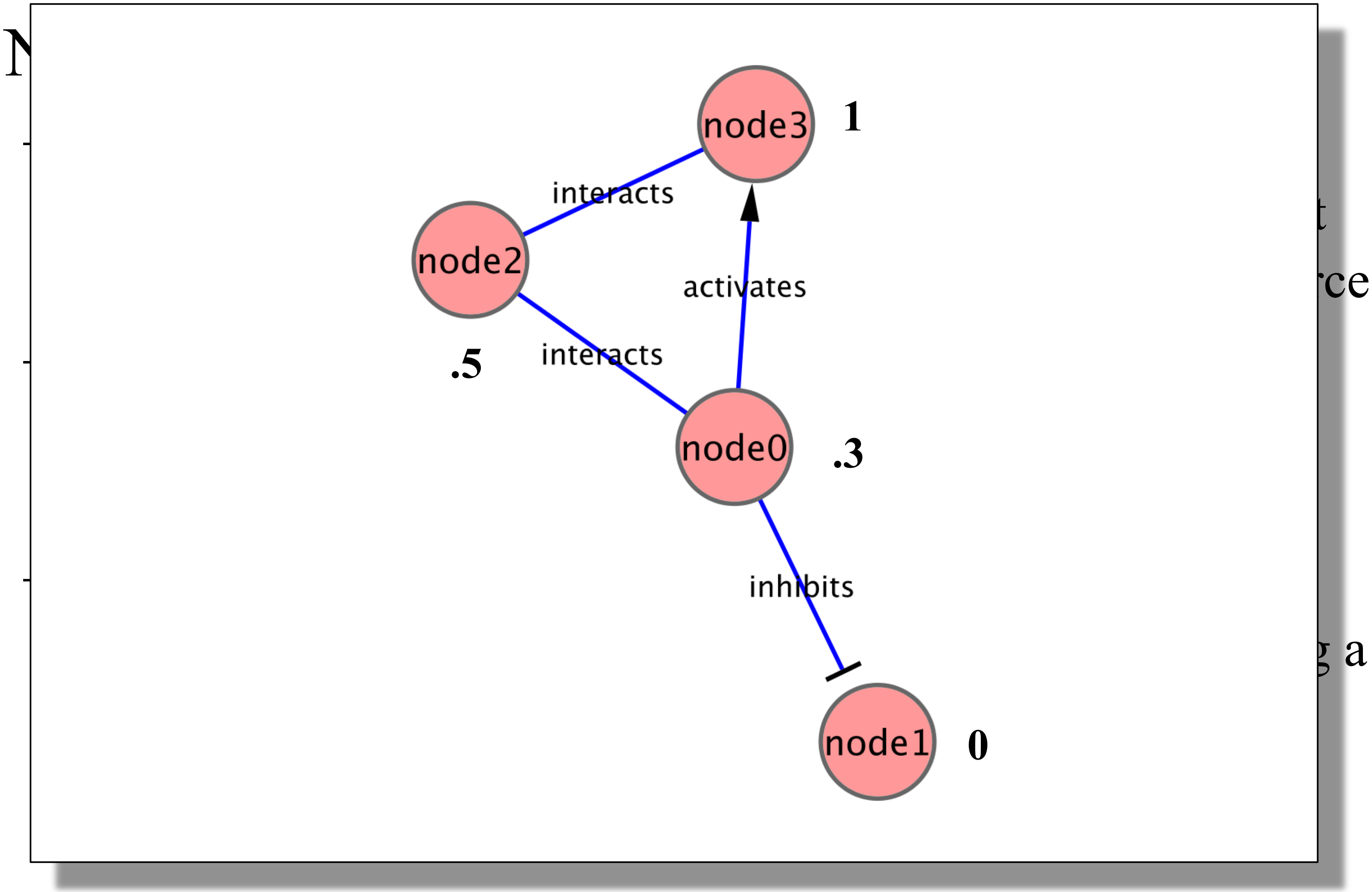

Analytical approaches

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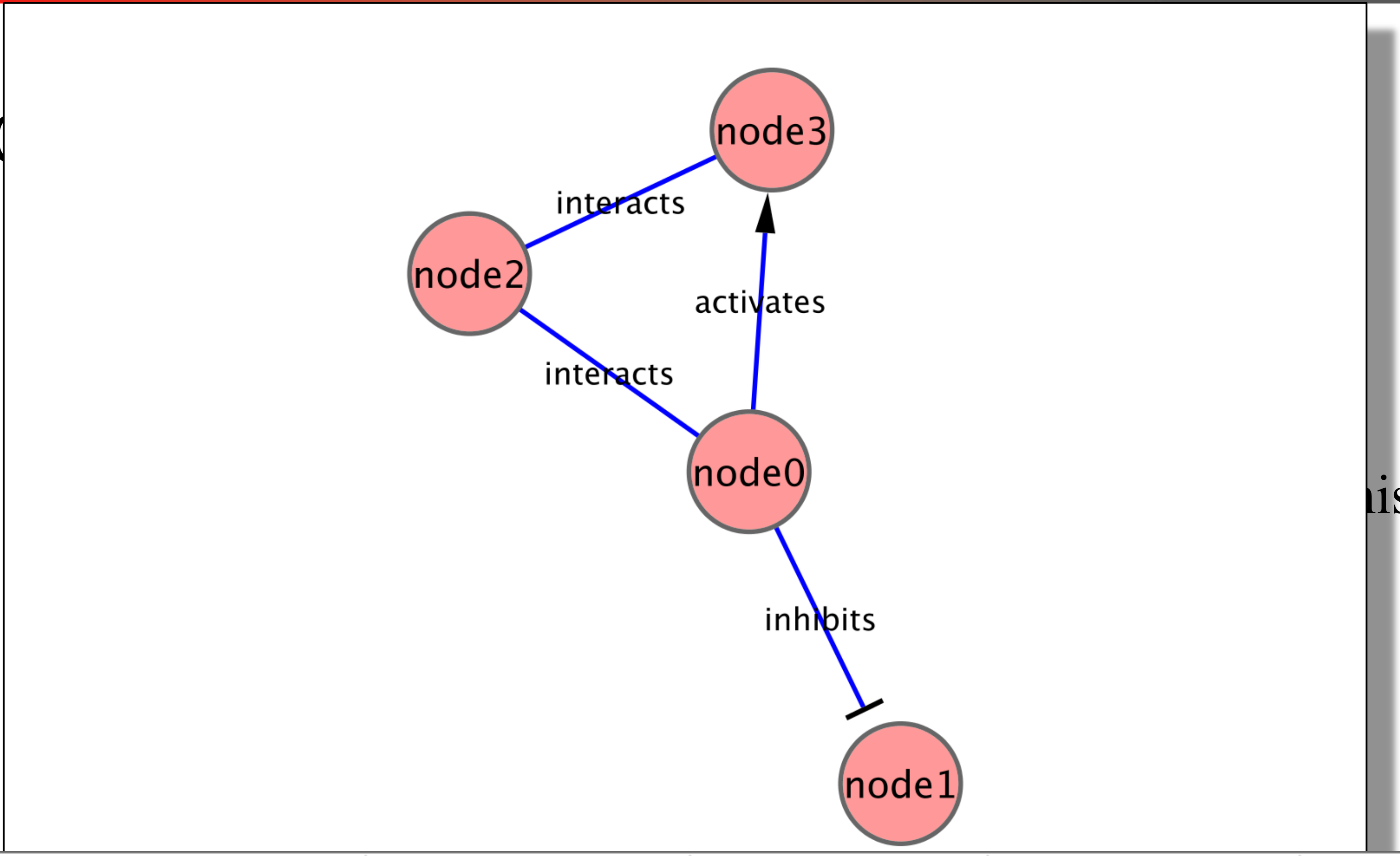
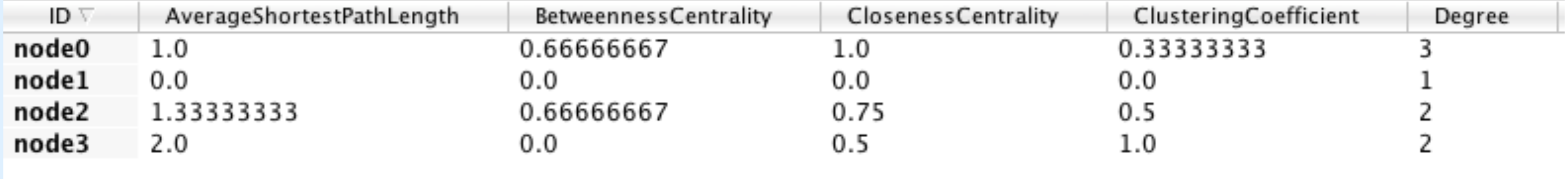
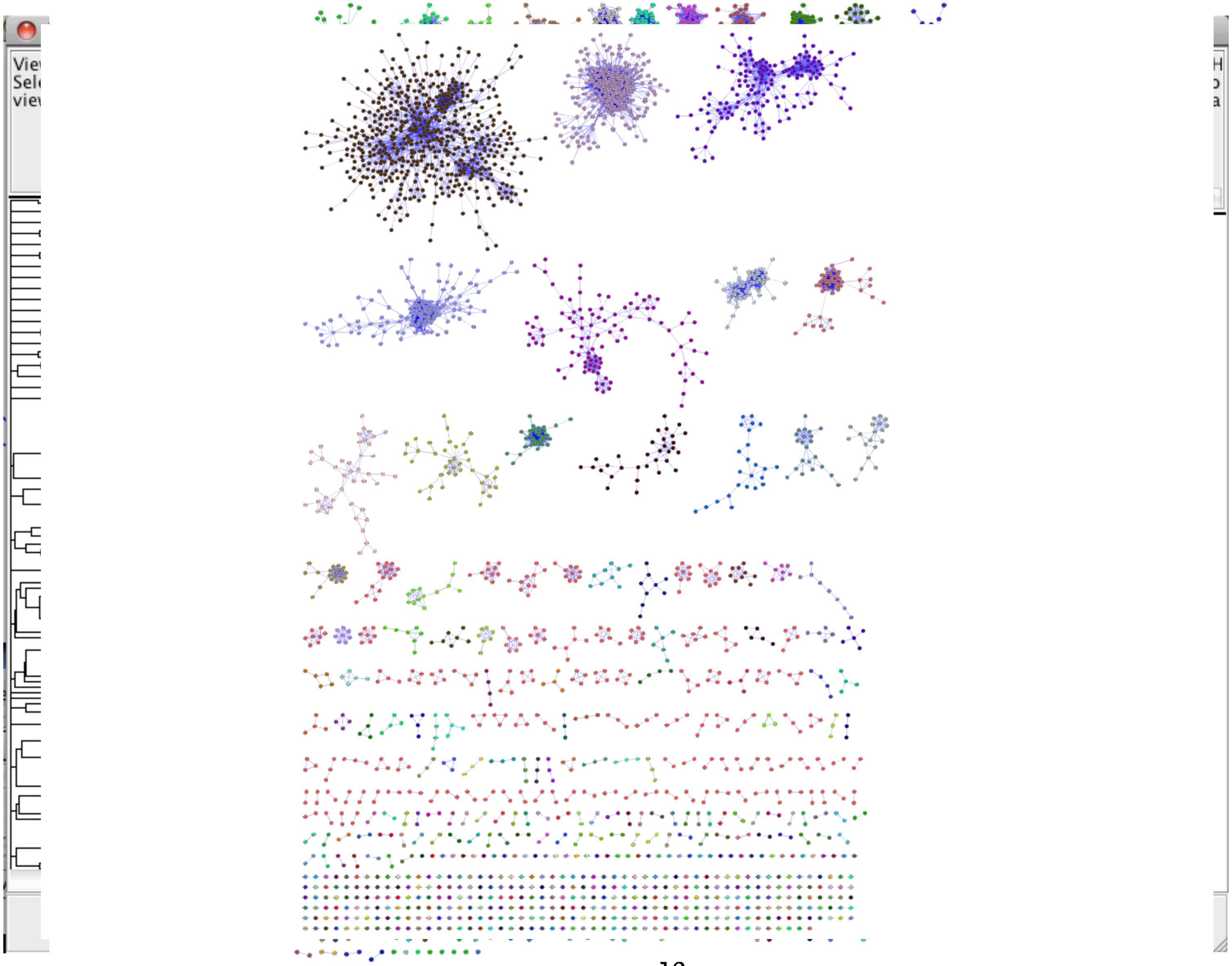




ID	AverageShortestPathLength	BetweennessCentrality	ClosenessCentrality	ClusteringCoefficient	Degree
node0	1.0	0.66666667	1.0	0.33333333	3
node1	0.0	0.0	0.0	0.0	1
node2	1.33333333	0.66666667	0.75	0.5	2
node3	2.0	0.0	0.5	1.0	2

Analytical approaches



Analytical approaches

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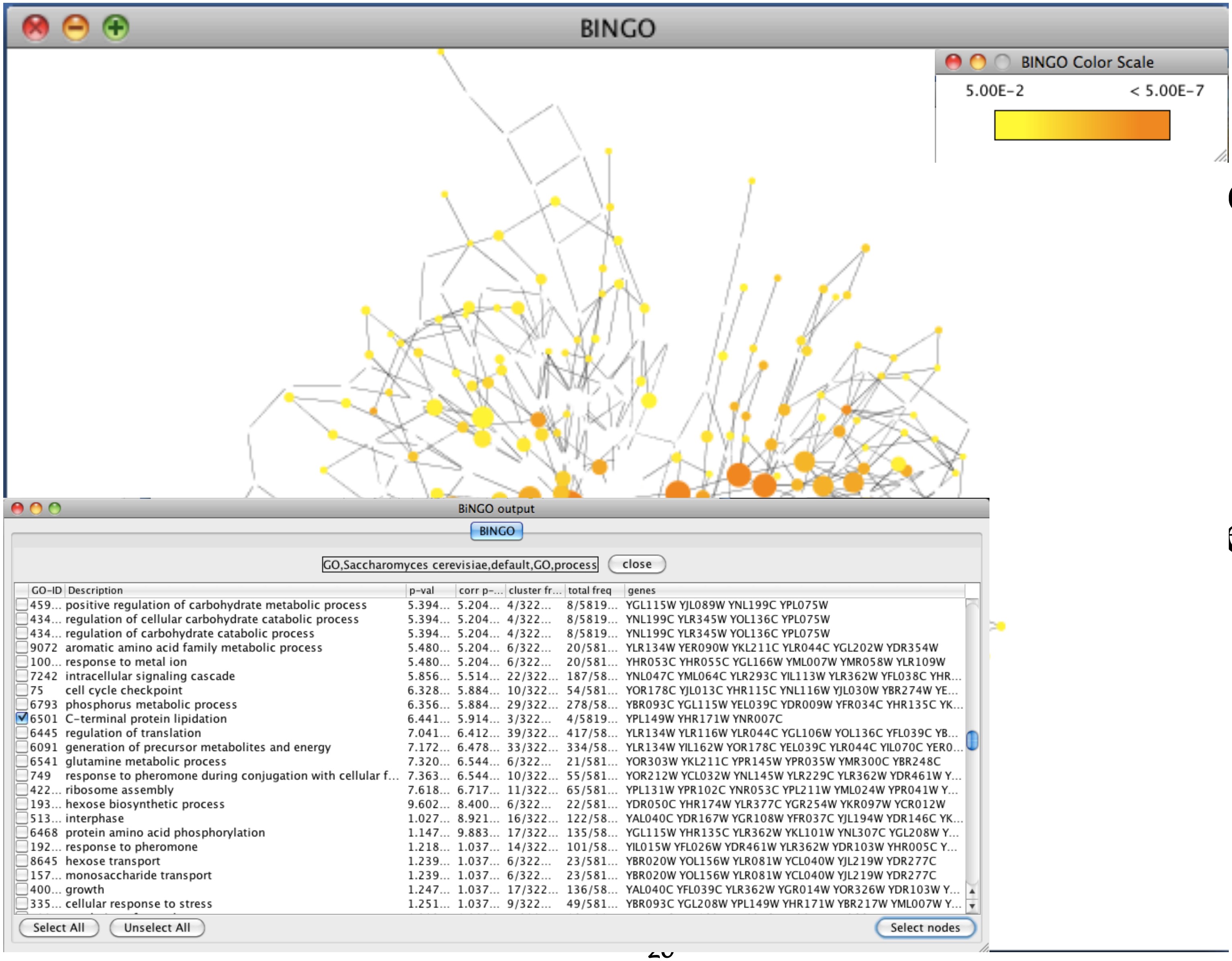


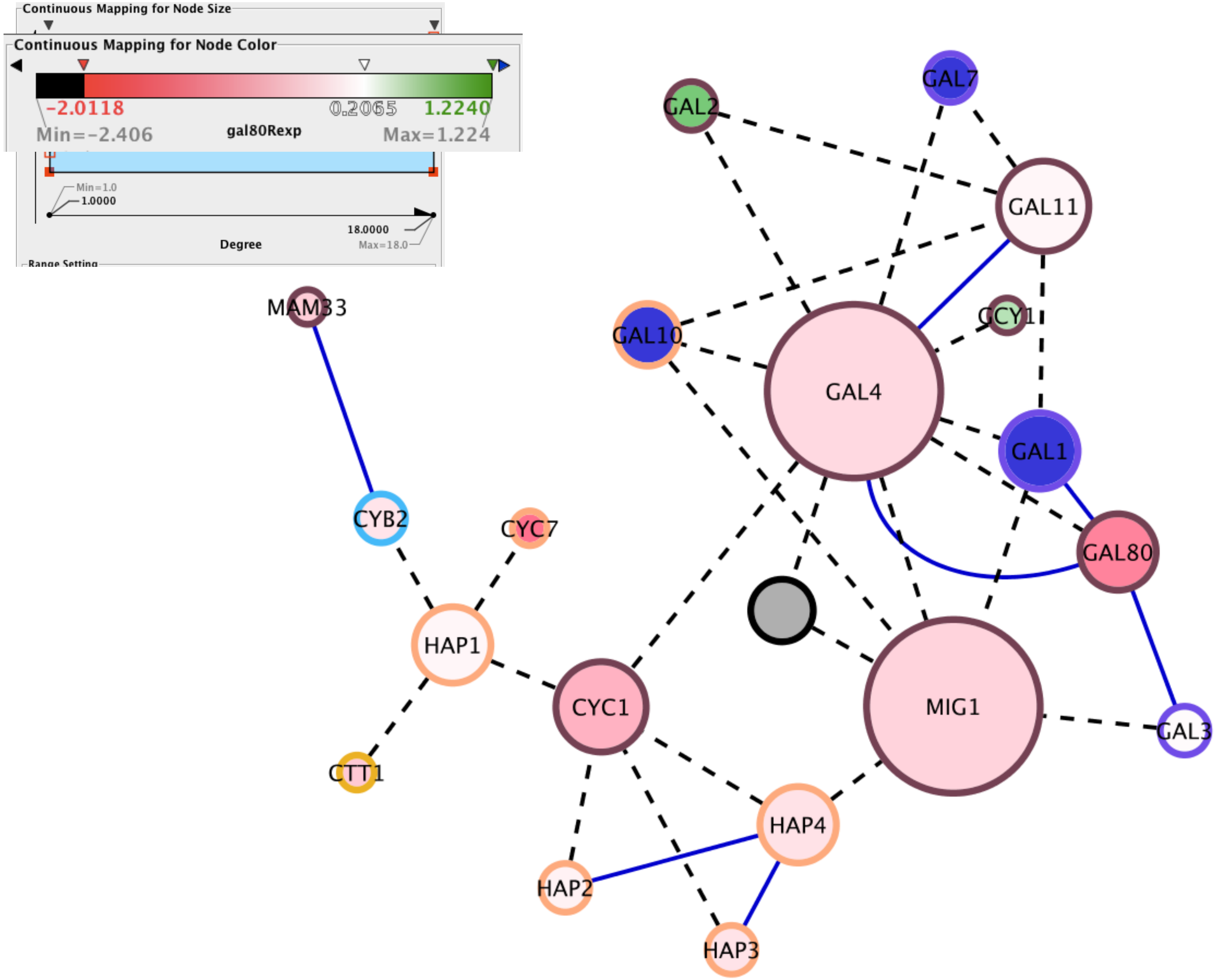
GO,Saccharomyces cerevisiae,default,GO,process

	GO-ID	Description	p-val	corr p-...	cluster fr...	total freq	genes
☐	459...	positive regulation of carbohydrate metabolic process	5.394...	5.204...	4/322...	8/5819...	YGL115W YJL089W YNL199C YPL075W
☐	434...	regulation of cellular carbohydrate catabolic process	5.394...	5.204...	4/322...	8/5819...	YNL199C YLR345W YOL136C YPL075W
☐	434...	regulation of carbohydrate catabolic process	5.394...	5.204...	4/322...	8/5819...	YNL199C YLR345W YOL136C YPL075W
☐	9072	aromatic amino acid family metabolic process	5.480...	5.204...	6/322...	20/581...	YLR134W YER090W YKL211C YLR044C YGL202W YDR354W
☐	100...	response to metal ion	5.480...	5.204...	6/322...	20/581...	YHR053C YHR055C YGL166W YML007W YMR058W YLR109W
☐	7242	intracellular signaling cascade	5.856...	5.514...	22/322...	187/58...	YNL047C YML064C YLR293C YIL113W YLR362W YFL038C YHR...
☐	75	cell cycle checkpoint	6.328...	5.884...	10/322...	54/581...	YOR178C YJL013C YHR115C YNL116W YJL030W YBR274W YE...
☐	6793	phosphorus metabolic process	6.356...	5.884...	29/322...	278/58...	YBR093C YGL115W YEL039C YDR009W YFR034C YHR135C YK...
☑	6501	C-terminal protein lipidation	6.441...	5.914...	3/322...	4/5819...	YPL149W YHR171W YNR007C
☐	6445	regulation of translation	7.041...	6.412...	39/322...	417/58...	YLR134W YLR116W YLR044C YGL106W YOL136C YFL039C YB...
☐	6091	generation of precursor metabolites and energy	7.172...	6.478...	33/322...	334/58...	YLR134W YIL162W YOR178C YEL039C YLR044C YIL070C YER0...
☐	6541	glutamine metabolic process	7.320...	6.544...	6/322...	21/581...	YOR303W YKL211C YPR145W YPR035W YMR300C YBR248C
☐	749	response to pheromone during conjugation with cellular f...	7.363...	6.544...	10/322...	55/581...	YOR212W YCL032W YNL145W YLR229C YLR362W YDR461W Y...
☐	422...	ribosome assembly	7.618...	6.717...	11/322...	65/581...	YPL131W YPR102C YNR053C YPL211W YML024W YPR041W Y...
☐	193...	hexose biosynthetic process	9.602...	8.400...	6/322...	22/581...	YDR050C YHR174W YLR377C YGR254W YKR097W YCR012W
☐	513...	interphase	1.027...	8.921...	16/322...	122/58...	YAL040C YDR167W YGR108W YFR037C YJL194W YDR146C YK...
☐	6468	protein amino acid phosphorylation	1.147...	9.883...	17/322...	135/58...	YGL115W YHR135C YLR362W YKL101W YNL307C YGL208W Y...
☐	192...	response to pheromone	1.218...	1.037...	14/322...	101/58...	YIL015W YFL026W YDR461W YLR362W YDR103W YHR005C Y...
☐	8645	hexose transport	1.239...	1.037...	6/322...	23/581...	YBR020W YOL156W YLR081W YCL040W YJL219W YDR277C
☐	157...	monosaccharide transport	1.239...	1.037...	6/322...	23/581...	YBR020W YOL156W YLR081W YCL040W YJL219W YDR277C
☐	400...	growth	1.247...	1.037...	17/322...	136/58...	YAL040C YFL039C YLR362W YGR014W YOR326W YDR103W Y...
☐	335...	cellular response to stress	1.251...	1.037...	9/322...	49/581...	YBR093C YGL208W YPL149W YHR171W YBR217W YML007W Y...

Visualisation approaches

- Data mapping
- Layouts
- Animation

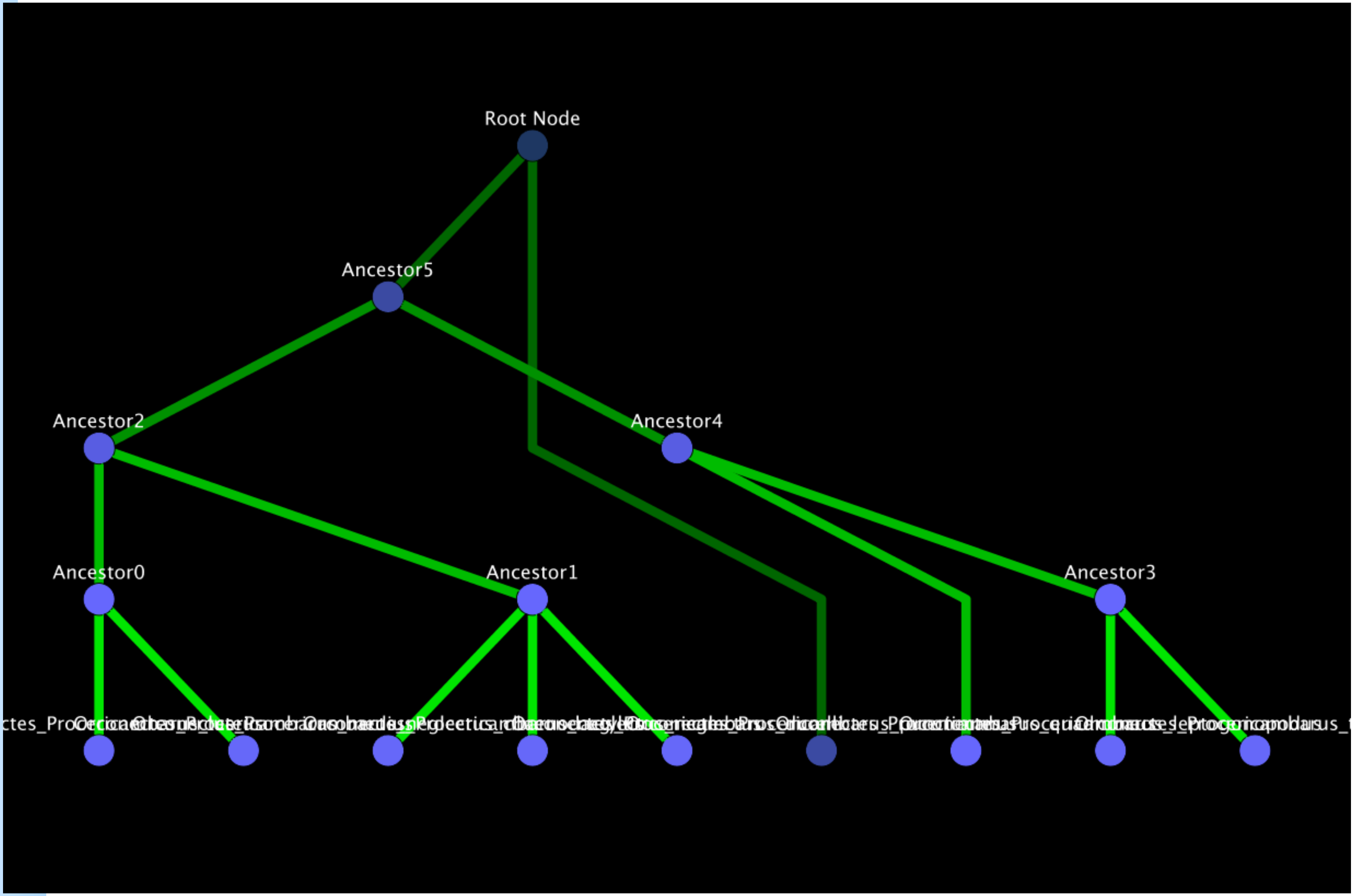
Data mapping



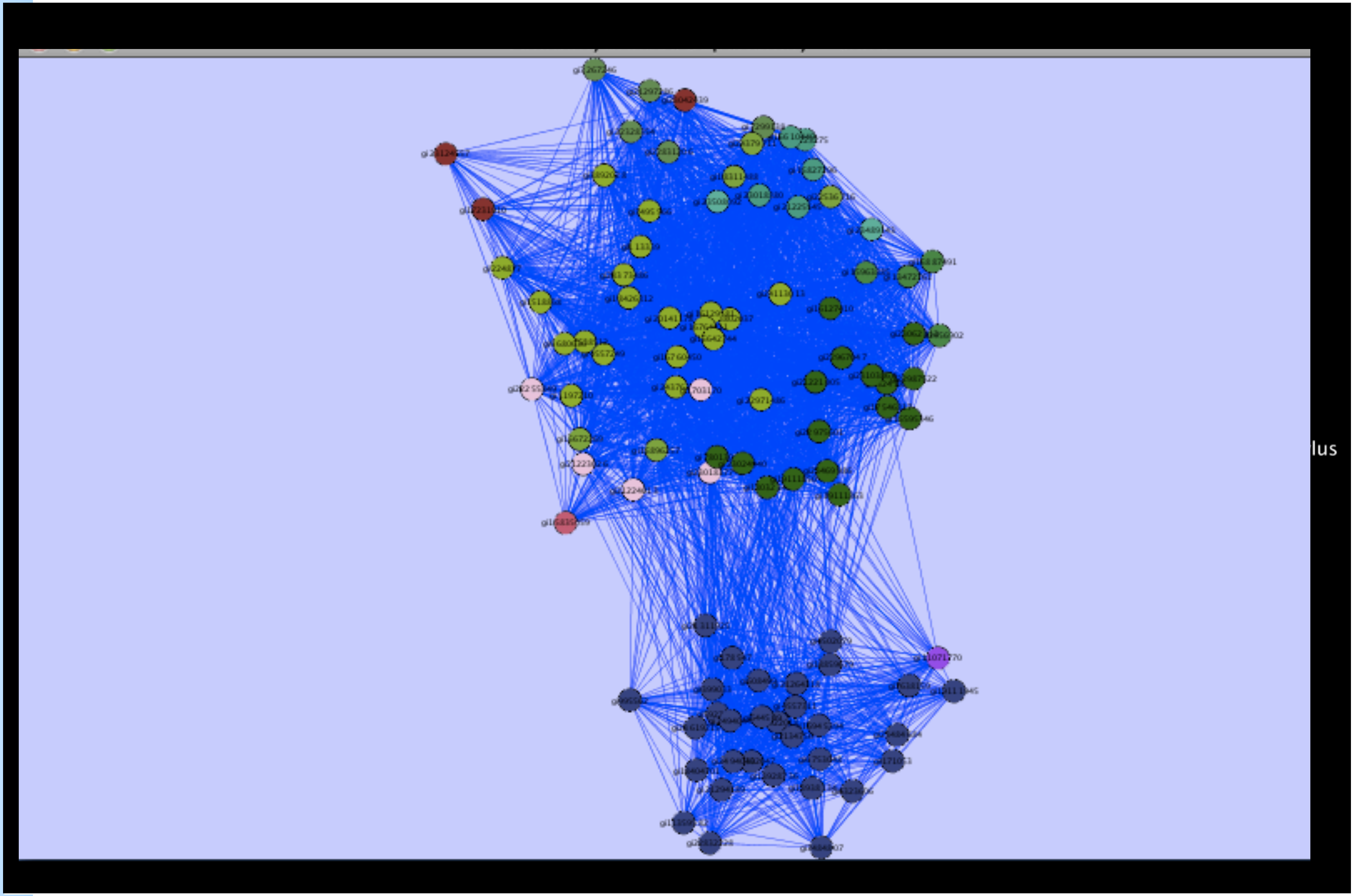
Data mapping

- Avoid cluttering your visualization with too much data
  - Map the data you are specifically interested in to call out meaningful differences
  - Mapping too much data to visual attributes may just confuse the viewer
  - Can always create multiple networks and map different values

Layouts


Root Node
Ancestor5
Ancestor2
Ancestor4
Ancestor0
Ancestor1
Ancestor3

Layouts



Layouts

- Use layouts to convey the true relationships between the nodes
- Layout algorithms may need to be “tuned” to fit your network
- Lots of parameters to change layout algorithm behavior
- Can also consider laying out portions of your network

Animation

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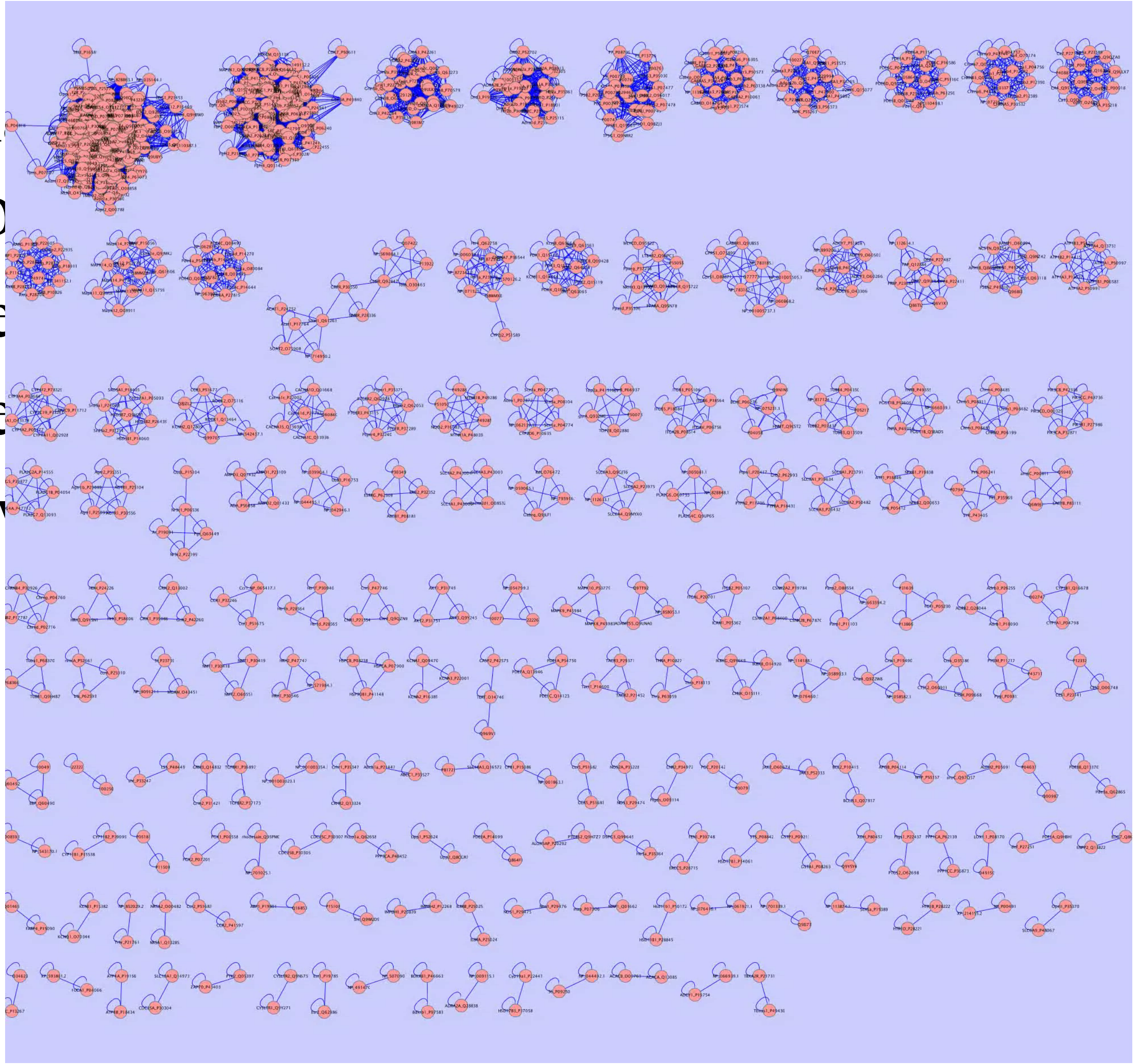
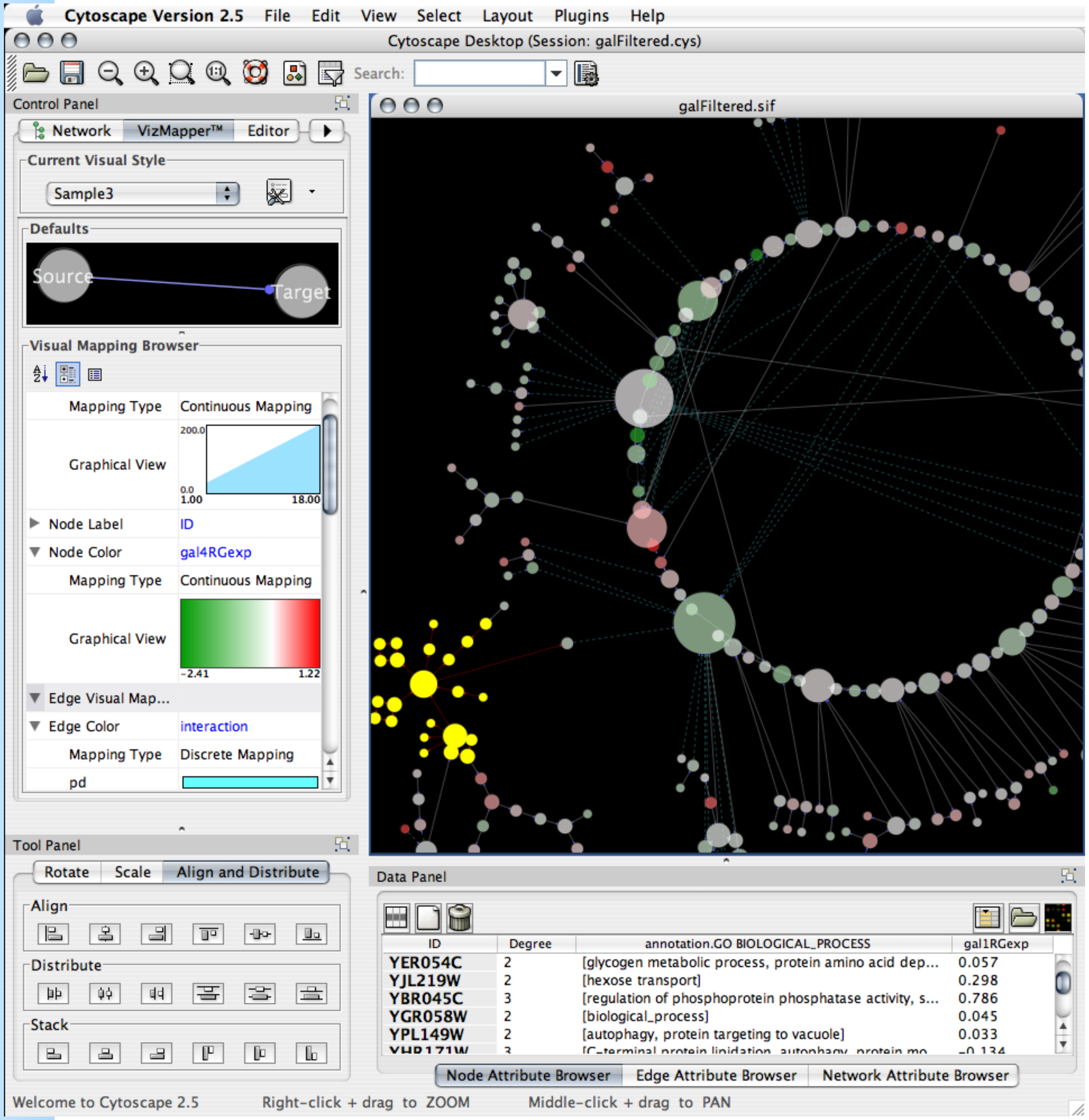


Cytoscape

- About 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." – Cytoscape Web Site

What is Cytoscape?



ID	Degree	annotation.GO BIOLOGICAL_PROCESS	gal1RGexp
YER054C	2	[glycogen metabolic process, protein amino acid dep...	0.057
YJL219W	2	[hexose transport]	0.298
YBR045C	3	[regulation of phosphoprotein phosphatase activity, s...	0.786
YGR058W	2	[biological_process]	0.045
YPL149W	2	[autophagy, protein targeting to vacuole]	0.033
YHR171W	3	[C-terminal protein lipidation, autophagy, protein mo...	-0.134

www.cytoscape.org

- Visualization
- Integration
- Analysis

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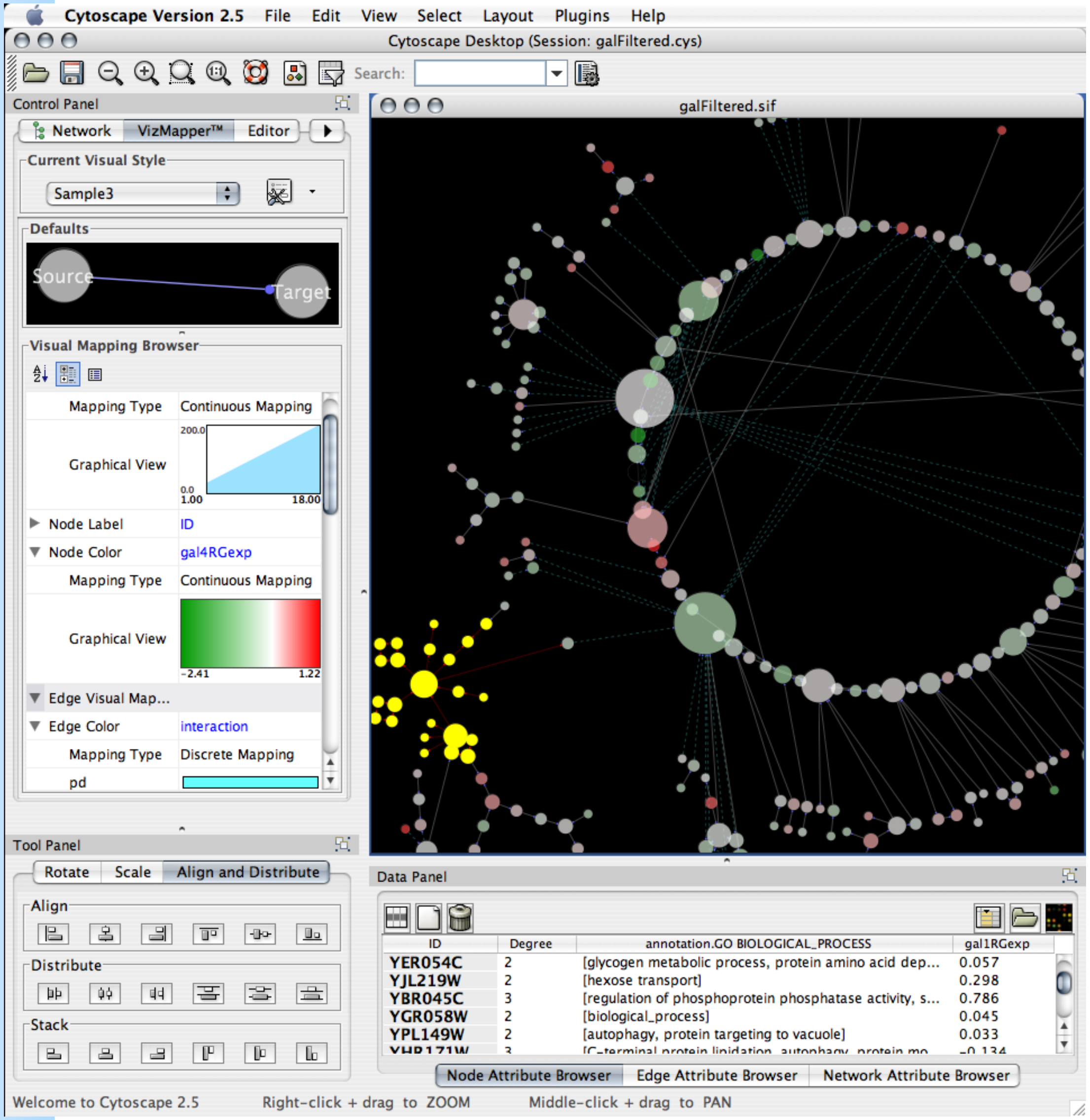

Current Visual Style: Sample3

Mapping Type: Continuous Mapping

Graphical View

Node Label: ID

Node Color: gal4RGexp

Mapping Type: Continuous Mapping

Graphical View

Edge Visual Map...

Edge Color: interaction

Mapping Type: Discrete Mapping

pd

ID	Degree	annotation.GO BIOLOGICAL_PROCESS	gal1RGexp
YER054C	2	[glycogen metabolic process, protein amino acid dep...	0.057
YJL219W	2	[hexose transport]	0.298
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Welcome to Cytoscape 2.5   Right-click + drag to ZOOM   Middle-click + drag to PAN

- Open source
- Cross platform
- A consortium

Institute for Systems Biology

University of California at San Diego

Memorial Sloan-Kettering Cancer Center

Institut Pasteur

Agilent Technologies

University of California at San Francisco

University of Toronto

University of Michigan

Unilever

Demonstration

- Cytoscape Demo
  - Vizmapper
  - clusterMaker
  - structureViz
  - chemViz

Questions?

- Thanks for your attention!

Workshop: Cytoscape

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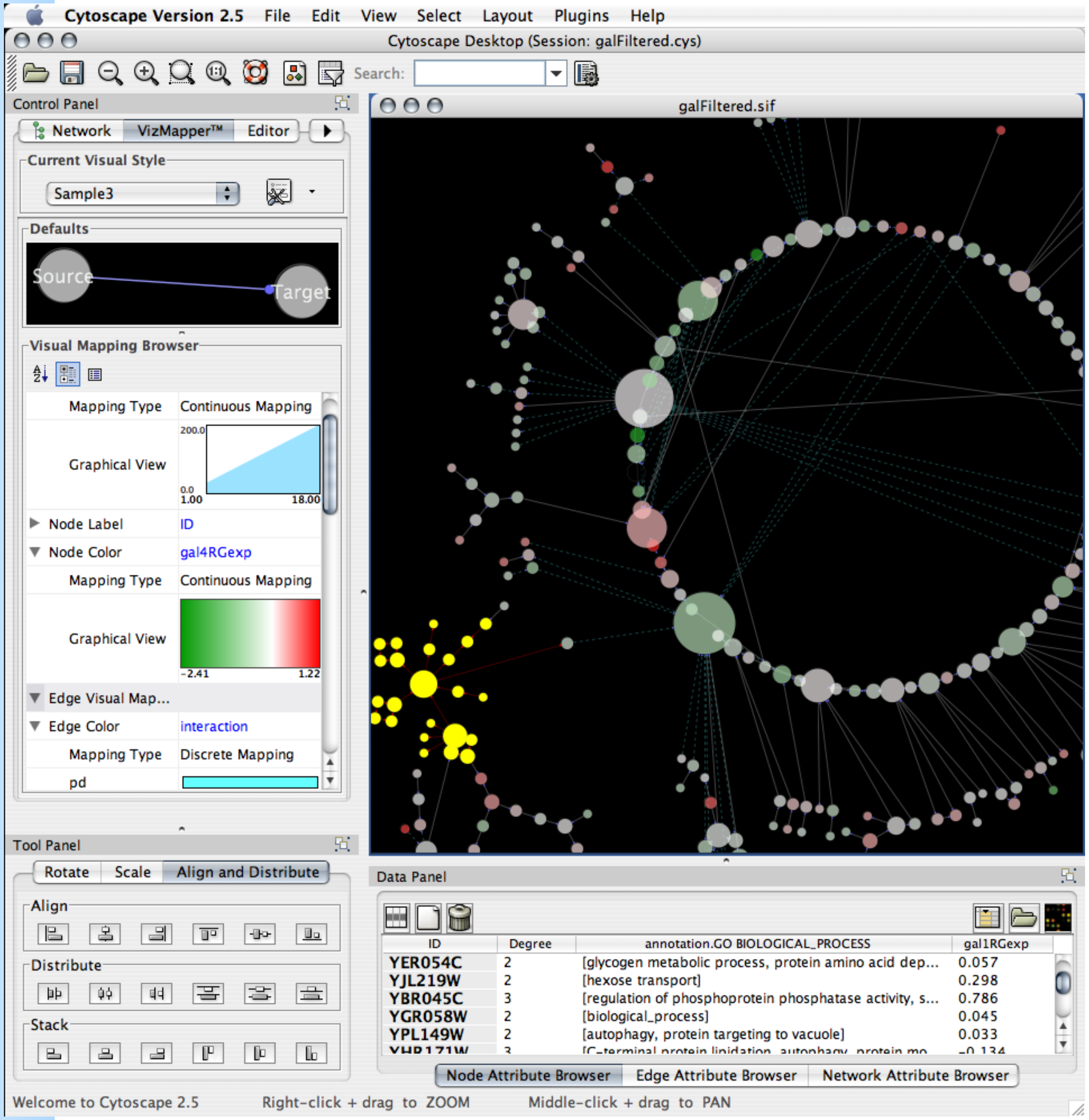

Current Visual Style: Sample3

Mapping Type: Continuous Mapping
Graphical View
Node Label: ID
Node Color: gal4RGexp
Mapping Type: Continuous Mapping
Graphical View
Edge Visual Map...
Edge Color: interaction
Mapping Type: Discrete Mapping
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www.cytoscape.org

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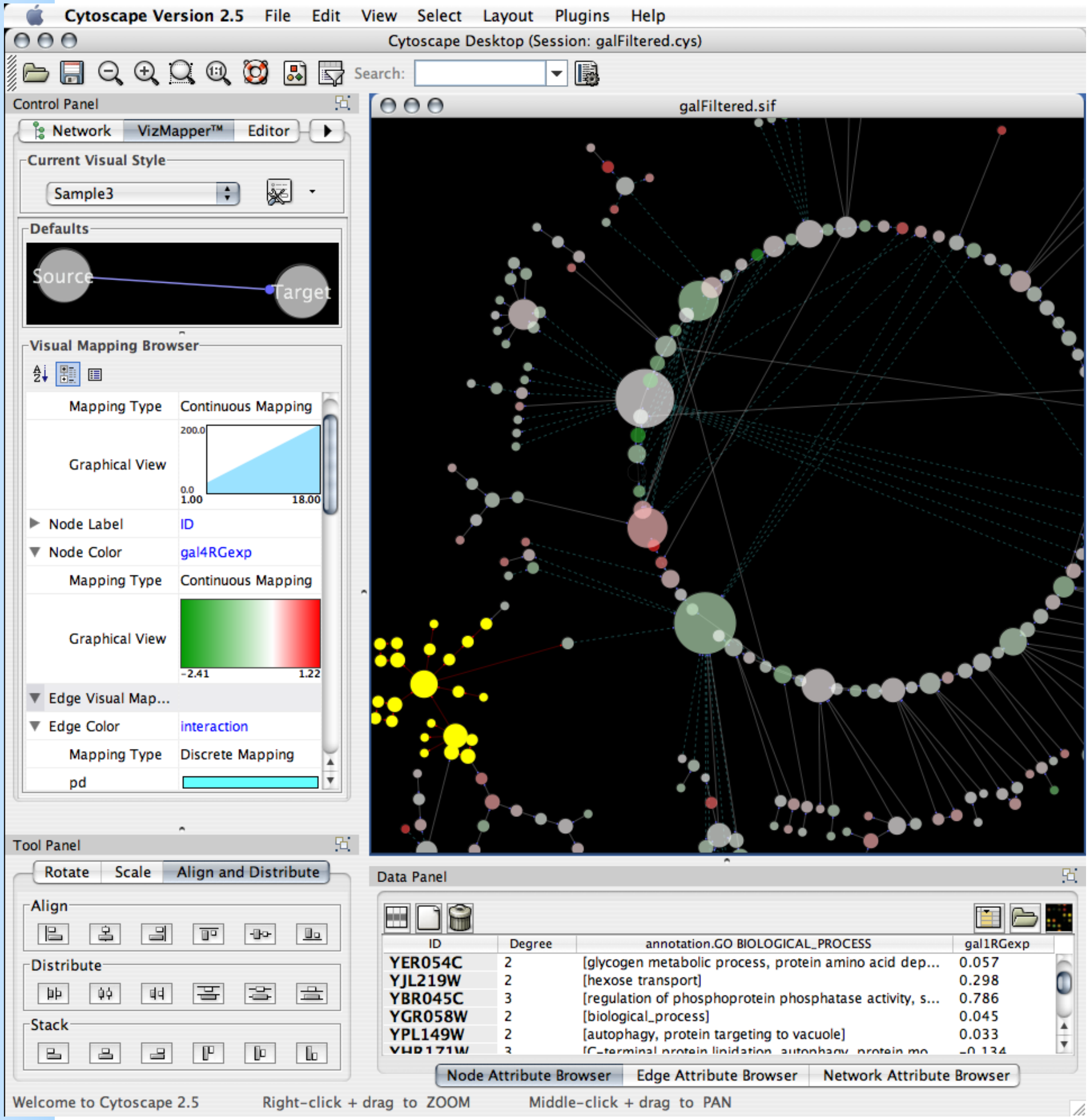

Current Visual Style: Sample3

Defaults

Visual Mapping Browser

Mapping Type	Continuous Mapping
Graphical View	
Node Label	ID
Node Color	gal4RGexp
Mapping Type	Continuous Mapping
Graphical View	
Edge Visual Map...	
Edge Color	interaction
Mapping Type	Discrete Mapping
pd	

ID	Degree	annotation.GO BIOLOGICAL_PROCESS	gal1RGexp
YER054C	2	[glycogen metabolic process, protein amino acid dep...	0.057
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- Cross platform
- A consortium
  - Institute for Systems Biology
  - University of California at San Diego
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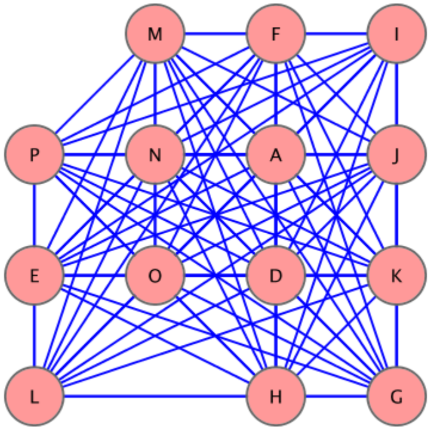
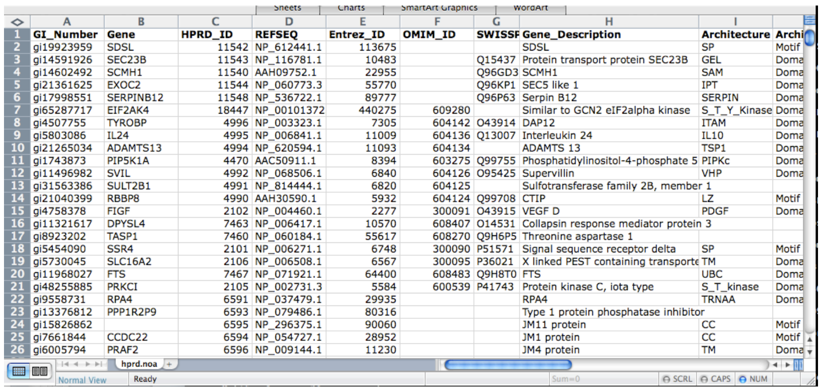
  - Agilent Technologies
  - University of California at San Francisco
  - University of Toronto
  - University of Michigan
  - Unilever

Core Concepts

- Networks and Annotations



Networks
e.g, biological pathways

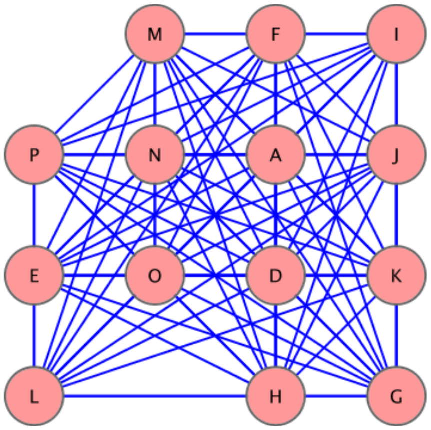


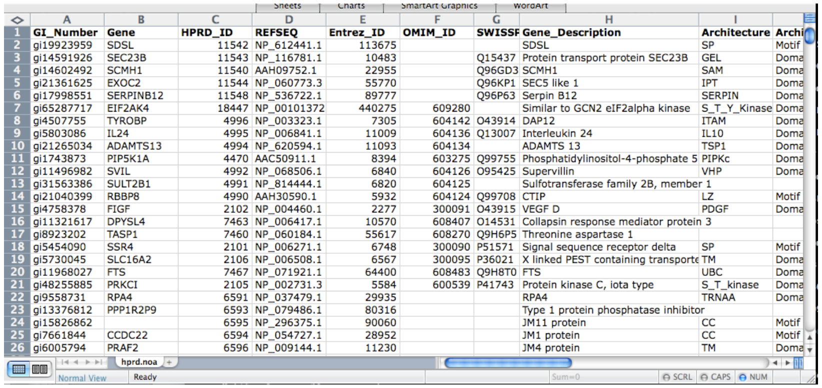
	A	B	C	D	E	F	G	H	I	
1	GI_Number	Gene	HPRD_ID	REFSEQ	Entrez_ID	OMIM_ID	SWISSP	Gene_Description	Architecture	Archi
2	gi19923959	SDSL	11542	NP_612441.1	113675			SDSL	SP	Motif
3	gi14591926	SEC23B	11543	NP_116781.1	10483		Q15437	Protein transport protein SEC23B	GEL	Doma
4	gi14602492	SCMH1	11540	AAH09752.1	22955		Q96GD3	SCMH1	SAM	Doma
5	gi21361625	EXOC2	11544	NP_060773.3	55770		Q96KP1	SEC5 like 1	IPT	Doma
6	gi17998551	SERPINB12	11548	NP_536722.1	89777		Q96P63	Serpin B12	SERPIN	Doma
7	gi65287717	EIF2AK4	18447	NP_00101372	440275	609280		Similar to GCN2 eIF2alpha kinase	S_T_Y_Kinase	Doma
8	gi4507755	TYROBP	4996	NP_003323.1	7305	604142	O43914	DAP12	ITAM	Doma
9	gi5803086	IL24	4995	NP_006841.1	11009	604136	Q13007	Interleukin 24	IL10	Doma
10	gi21265034	ADAMTS13	4994	NP_620594.1	11093	604134		ADAMTS 13	TSP1	Doma
11	gi1743873	PIP5K1A	4470	AAC50911.1	8394	603275	Q99755	Phosphatidylinositol-4-phosphate 5	PIPKc	Doma
12	gi11496982	SVIL	4992	NP_068506.1	6840	604126	O95425	Supervillin	VHP	Doma
13	gi31563386	SULT2B1	4991	NP_814444.1	6820	604125		Sulfotransferase family 2B, member 1		
14	gi21040399	RBBP8	4990	AAH30590.1	5932	604124	Q99708	CTIP	LZ	Motif
15	gi4758378	FIGF	2102	NP_004460.1	2277	300091	O43915	VEGF D	PDGF	Doma
16	gi11321617	DPYSL4	7463	NP_006417.1	10570	608407	O14531	Collapsin response mediator protein 3		
17	gi8923202	TASP1	7460	NP_060184.1	55617	608270	Q9H6P5	Threonine aspartase 1		
18	gi5454090	SSR4	2101	NP_006271.1	6748	300090	P51571	Signal sequence receptor delta	SP	Motif
19	gi5730045	SLC16A2	2106	NP_006508.1	6567	300095	P36021	X linked PEST containing transporte	TM	Doma
20	gi11968027	FTS	7467	NP_071921.1	64400	608483	Q9H8T0	FTS	UBC	Doma
21	gi48255885	PRKCI	2105	NP_002731.3	5584	600539	P41743	Protein kinase C, iota type	S_T_kinase	Doma
22	gi9558731	RPA4	6591	NP_037479.1	29935			RPA4	TRNAA	Doma
23	gi13376812	PPP1R2P9	6593	NP_079486.1	80316			Type 1 protein phosphatase inhibitor		
24	gi15826862		6595	NP_296375.1	90060			JM11 protein	CC	Motif
25	gi7661844	CCDC22	6594	NP_054727.1	28952			JM1 protein	CC	Motif
26	gi6005794	PRAF2	6596	NP_009144.1	11230			JM4 protein	TM	Doma

Annotations
e.g., attributes or data

Core Concepts

- Visual Mapping with VizMapper





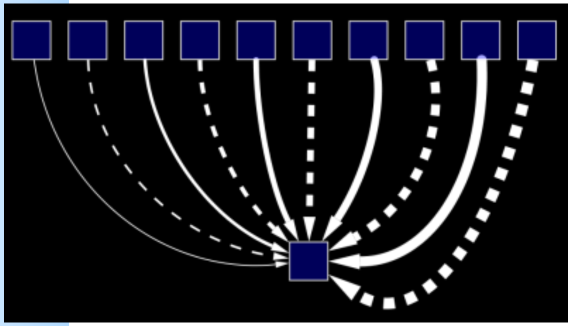
	A	B	C	D	E	F	G	H	I	
1	**GI_Number**	**Gene**	**HPRD_ID**	**REFSEQ**	**Entrez_ID**	**OMIM_ID**	**SWISSF**	**Gene_Description**	**Architecture**	**Archi**
2	gi19923959	SDSL	11542	NP_612441.1	113675			SDSL	SP	Motif
3	gi14591926	SEC23B	11543	NP_116781.1	10483		Q15437	Protein transport protein SEC23B	GEL	Doma
4	gi14602492	SCMH1	11540	AAH09752.1	22955		Q96GD3	SCMH1	SAM	Doma
5	gi21361625	EXOC2	11544	NP_060773.3	55770		Q96KP1	SEC5 like 1	IPT	Doma
6	gi17998551	SERPINB12	11548	NP_536722.1	89777		Q96P63	Serpin B12	SERPIN	Doma
7	gi65287717	EIF2AK4	18447	NP_00101372	440275	609280		Similar to GCN2 eIF2alpha kinase	S_T_Y_Kinase	Doma
8	gi4507755	TYROBP	4996	NP_003323.1	7305	604142	O43914	DAP12	ITAM	Doma
9	gi5803086	IL24	4995	NP_006841.1	11009	604136	Q13007	Interleukin 24	IL10	Doma
10	gi21265034	ADAMTS13	4994	NP_620594.1	11093	604134		ADAMTS 13	TSP1	Doma
11	gi1743873	PIP5K1A	4470	AAC50911.1	8394	603275	Q99755	Phosphatidylinositol-4-phosphate 5	PIPKc	Doma
12	gi11496982	SVIL	4992	NP_068506.1	6840	604126	O95425	Supervillin	VHP	Doma
13	gi31563386	SULT2B1	4991	NP_814444.1	6820	604125		Sulfotransferase family 2B, member 1		
14	gi21040399	RBBP8	4990	AAH30590.1	5932	604124	Q99708	CTIP	LZ	Motif
15	gi4758378	FIGF	2102	NP_004460.1	2277	300091	O43915	VEGF D	PDGF	Doma
16	gi11321617	DPYSL4	7463	NP_006417.1	10570	608407	O14531	Collapsin response mediator protein 3		
17	gi8923202	TASP1	7460	NP_060184.1	55617	608270	Q9H6P5	Threonine aspartase 1		
18	gi5454090	SSR4	2101	NP_006271.1	6748	300090	P51571	Signal sequence receptor delta	SP	Motif
19	gi5730045	SLC16A2	2106	NP_006508.1	6567	300095	P36021	X linked PEST containing transporte	TM	Doma
20	gi11968027	FTS	7467	NP_071921.1	64400	608483	Q9H8T0	FTS	UBC	Doma
21	gi48255885	PRKCI	2105	NP_002731.3	5584	600539	P41743	Protein kinase C, iota type	S_T_kinase	Doma
22	gi9558731	RPA4	6591	NP_037479.1	29935			RPA4	TRNAA	Doma
23	gi13376812	PPP1R2P9	6593	NP_079486.1	80316			Type 1 protein phosphatase inhibitor		
24	gi15826862		6595	NP_296375.1	90060			JM11 protein	CC	Motif
25	gi7661844	CCDC22	6594	NP_054727.1	28952			JM1 protein	CC	Motif
26	gi6005794	PRAF2	6596	NP_009144.1	11230			JM4 protein	TM	Doma

Networks

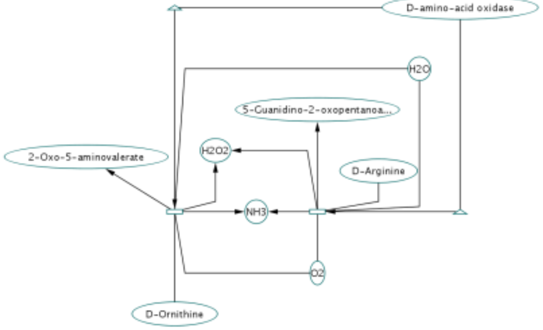
Annotations

VizMapper

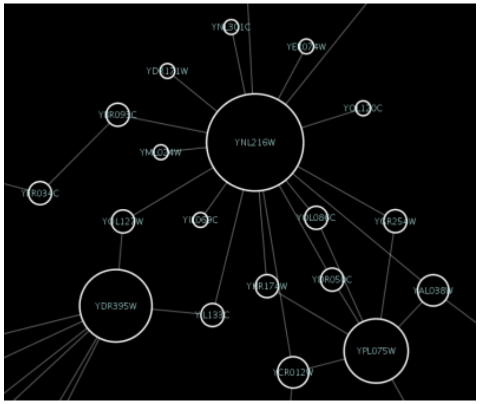
Visual Styles



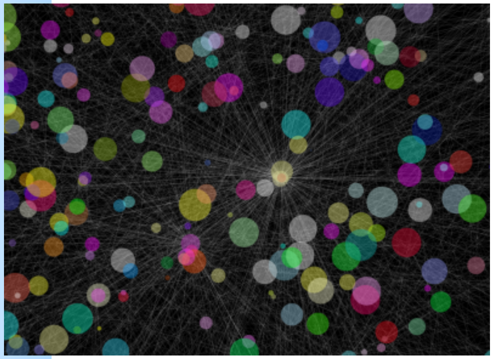
Use specific line types to indicate different types of interactions



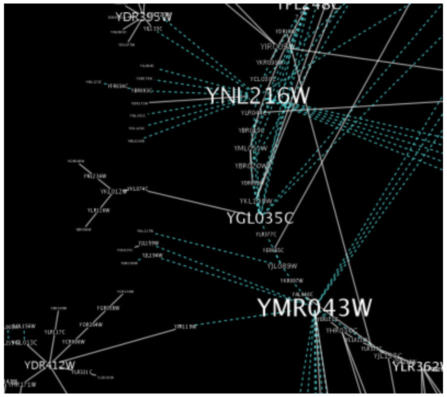
Encode specific physical entities as different node shapes.



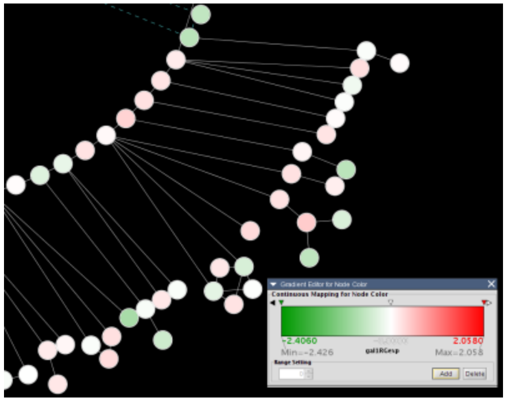
Set node sizes based on the degree of connectivity of the nodes.



Browse extremely dense networks by controlling for the opacity of nodes



Set node font sizes based on the degree of connectivity of the nodes.



Expression data

Core Concepts

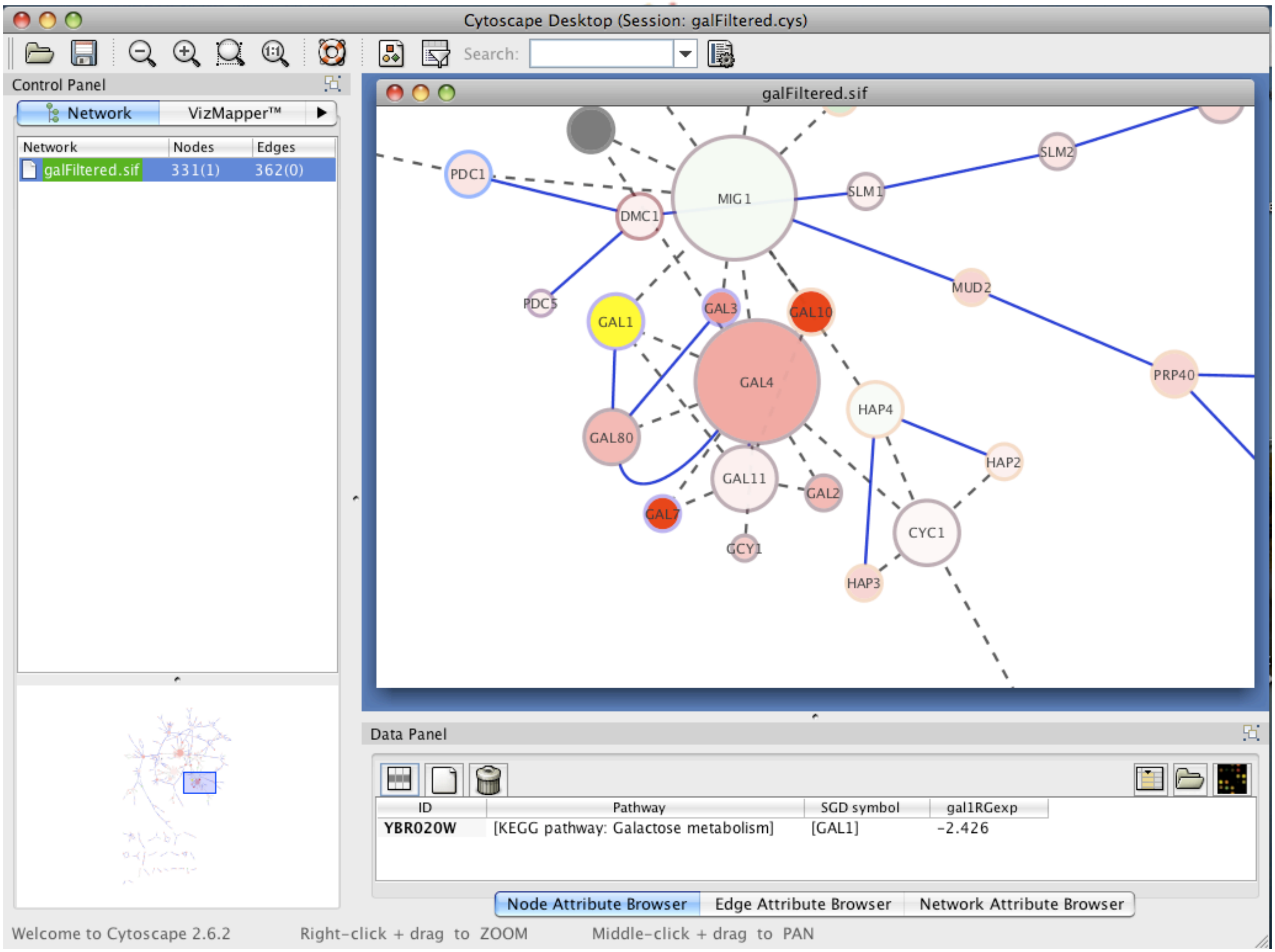
- Plugins!

http://chianti.ucsd.edu/cyto_web/plugins/index.php

Cytoscape

- Traditional uses
  - Visualizing:
    - PPI
    - Pathways
  - Mapping:
    - Expression profiles
    - “Other state data”

Cytoscape



Cytoscape Desktop (Session: galFiltered.cys)

Network	Nodes	Edges
galFiltered.sif	331(1)	362(0)

galFiltered.sif

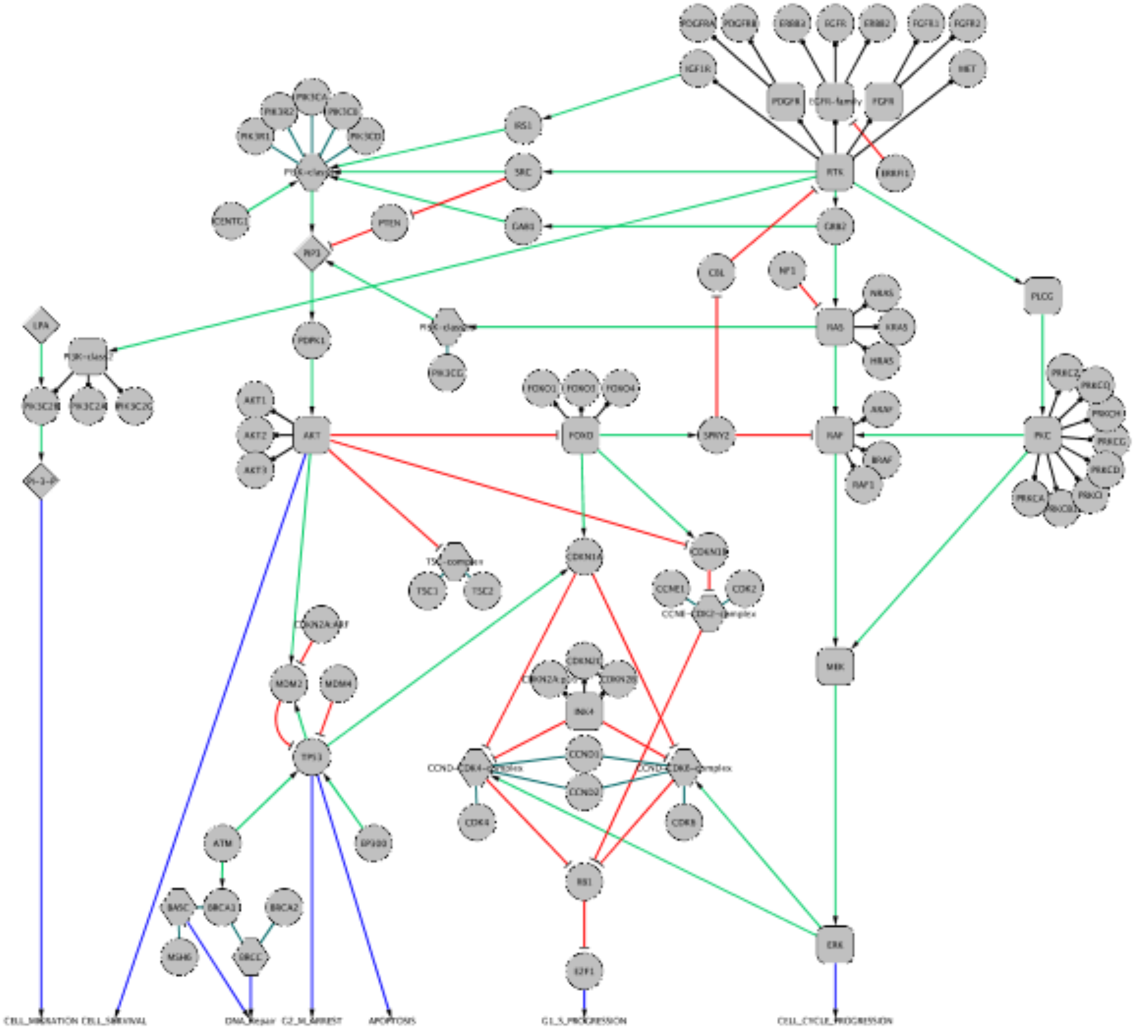
ID	Pathway	SGD symbol	gal1RGexp
YBR020W	[KEGG pathway: Galactose metabolism]	[GAL1]	-2.426

Welcome to Cytoscape 2.6.2

Right-click + drag to ZOOM

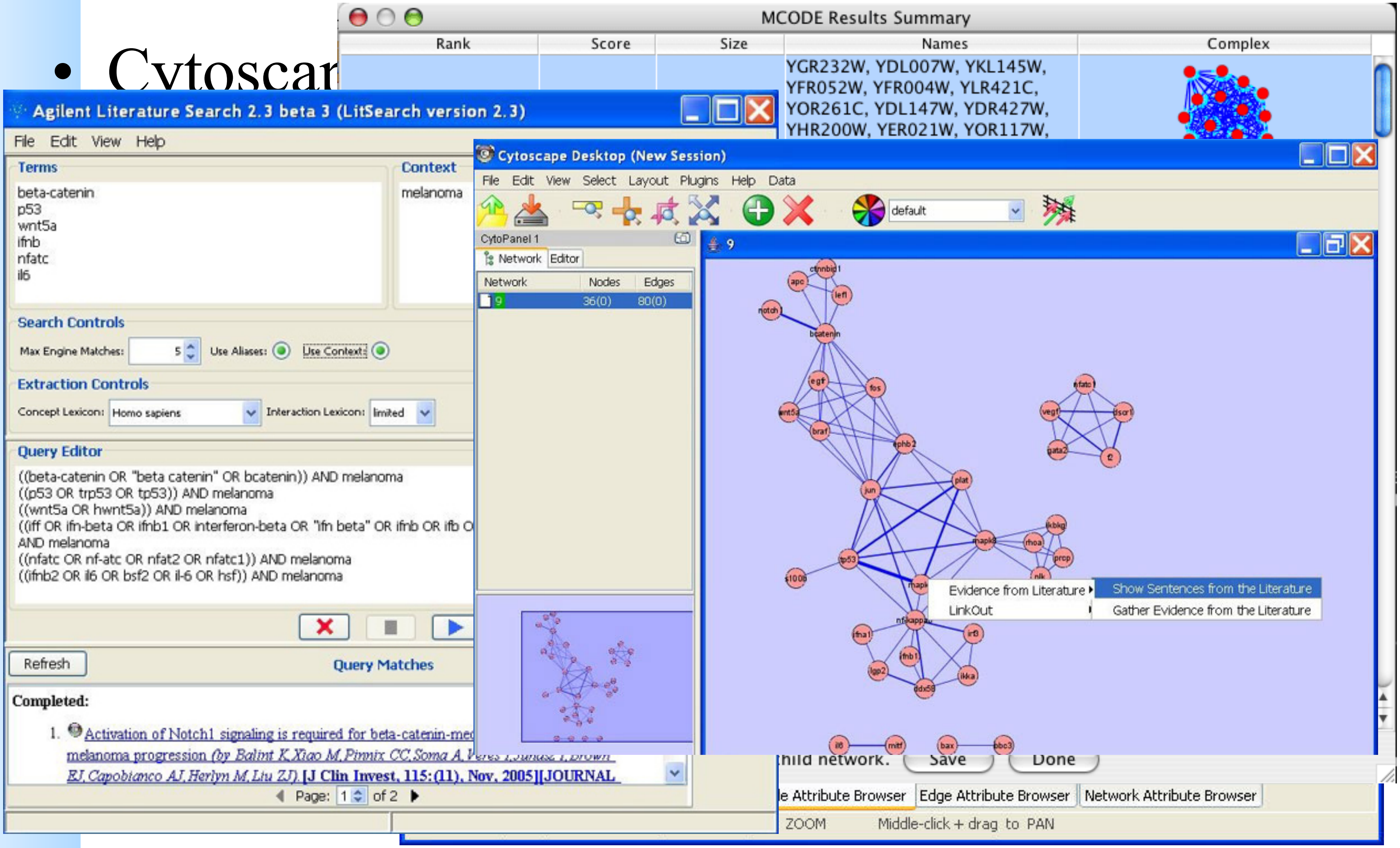
Middle-click + drag to PAN

Cytoscape


PDGFRA
PDGFRB
ERBB3
EGFR
ERBB2
FGFR1
FGFR2
IGF1R
MET
PDGFR
EGFR-family
FGFR
RTK
ERRFI1
IRS1
SRC
GAB1
GRB2
PIK3CA
PIK3R2
PIK3CB
PIK3R1
PIK3CD
PI3K-class1
CENTG1
PTEN
PIP3
CBL
NF1
PLCG
NRAS
KRAS
HRAS
RAS
LPA
PI3K-class2
PI3K-class1B
PIK3CG
PDPK1
PIK3C2B
PIK3C2A
PIK3C2G
PI-3-P
AKT1
AKT2
AKT3
AKT
FOXO1
FOXO3
FOXO4
FOXO
SPRY2
ARAF
RAF
BRAF
RAF1
PKC
PRKCZ
PRKCQ
PRKCH
PRKCG
PRKCD
PRKCI
PRKCA
PRKCB1
TSC-complex
TSC1
TSC2
CDKN1A
CDKN1B
CCNE1
CDK2
CCNE-CDK2-complex
MEK
CDKN2A.ARF
MDM2
MDM4
CDKN2C
CDKN2A.p16
CDKN2B
INK4
TP53
CCND1
CCND2
CCND-CDK4-complex
CCND-CDK6-complex
CDK4
CDK6
ATM
EP300
BASC
BRCA1
BRCA2
MSH6
BRCC
RB1
E2F1
ERK
CELL_MIGRATION
CELL_SURVIVAL
DNA_Repair
G2_M_ARREST
APOPTOSIS
G1_S_PROGRESSION
CELL_CYCLE_PROGRESSION

Cytoscape: Platform

- Cytoscap



MCODE Results Summary

Rank	Score	Size	Names	Complex
			YGR232W, YDL007W, YKL145W, YFR052W, YFR004W, YLR421C, YOR261C, YDL147W, YDR427W, YHR200W, YER021W, YOR117W,	

Agilent Literature Search 2.3 beta 3 (LitSearch version 2.3)

Terms

beta-catenin
p53
wnt5a
ifnb
nfatc
il6

Context

melanoma

Search Controls

Max Engine Matches: 5 Use Aliases: ● Use Context: ●

Extraction Controls

Concept Lexicon: Homo sapiens Interaction Lexicon: limited

Query Editor

((beta-catenin OR "beta catenin" OR bcatenin)) AND melanoma
((p53 OR trp53 OR tp53)) AND melanoma
((wnt5a OR hwnt5a)) AND melanoma
((iff OR ifn-beta OR ifnb1 OR interferon-beta OR "ifn beta" OR ifnb OR ifb O
AND melanoma
((nfatc OR nf-atc OR nfat2 OR nfatc1)) AND melanoma
((ifnb2 OR il6 OR bsf2 OR il-6 OR hsf)) AND melanoma

Query Matches

Completed:

1. Activation of Notch1 signaling is required for beta-catenin-med melanoma progression (by Balint K,Xiao M,Pinnix CC,Soma A,Veres I,Juhasz I,Brown EJ,Capobianco AJ,Herlyn M,Liu ZJ) [J Clin Invest, 115:(11), Nov, 2005][JOURNAL

Page: 1 of 2

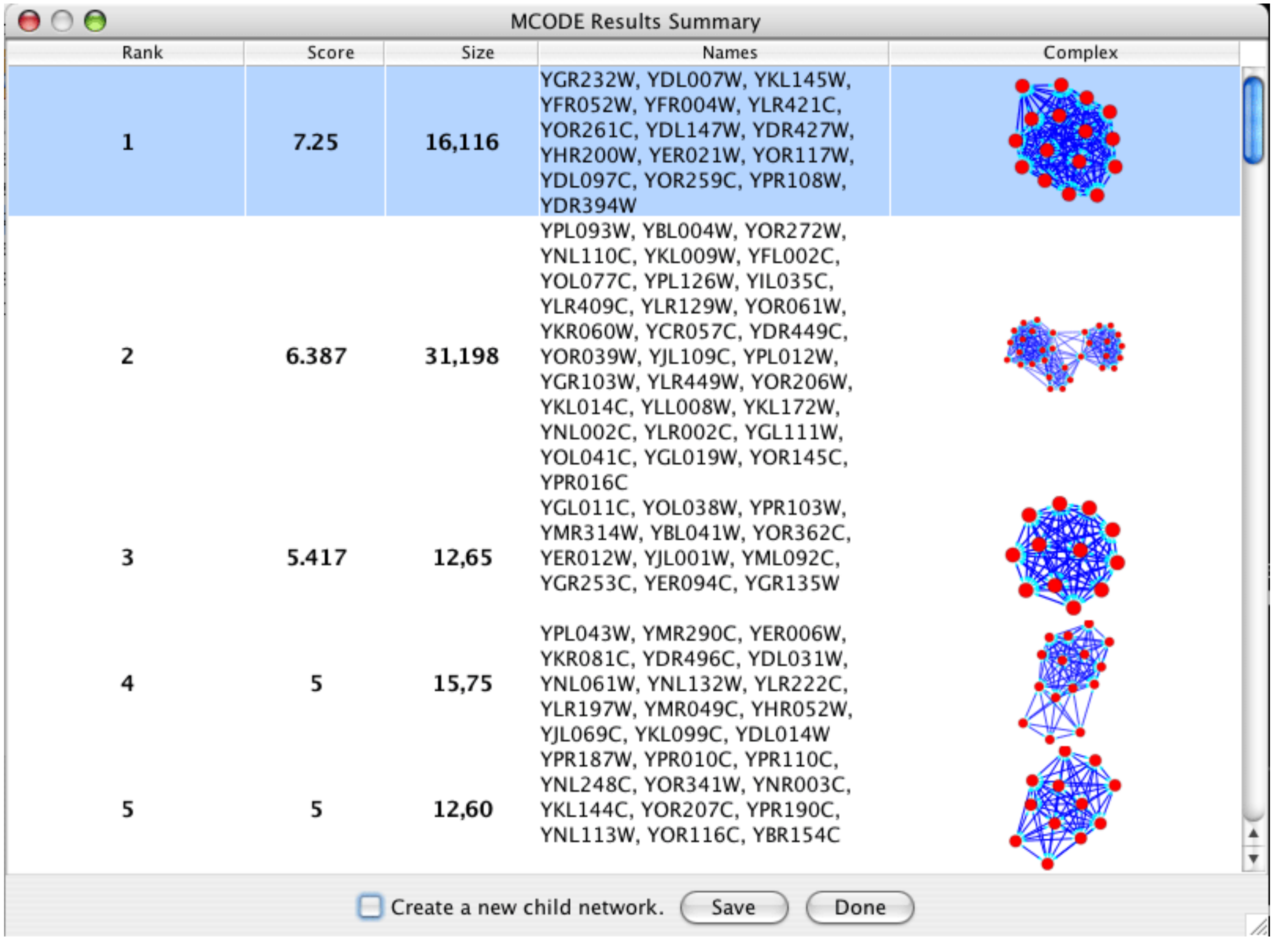
Cytoscape Desktop (New Session)

Network	Nodes	Edges
9	36(0)	80(0)

ZOOM Middle-click + drag to PAN

Plugins

- MCODE



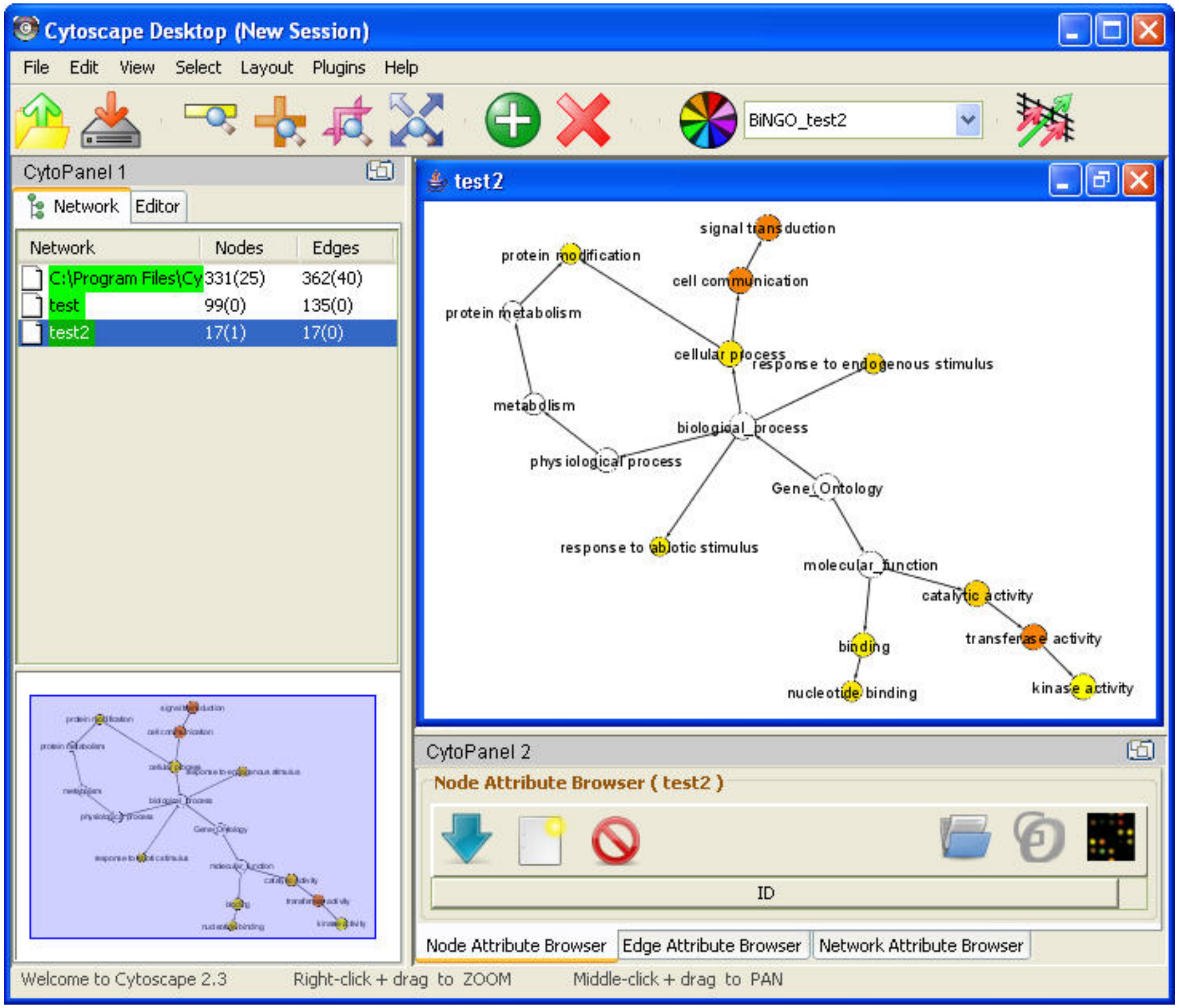
MCODE Results Summary

Rank	Score	Size	Names	Complex
1	7.25	16,116	YGR232W, YDL007W, YKL145W, YFR052W, YFR004W, YLR421C, YOR261C, YDL147W, YDR427W, YHR200W, YER021W, YOR117W, YDL097C, YOR259C, YPR108W, YDR394W	
2	6.387	31,198	YPL093W, YBL004W, YOR272W, YNL110C, YKL009W, YFL002C, YOL077C, YPL126W, YIL035C, YLR409C, YLR129W, YOR061W, YKR060W, YCR057C, YDR449C, YOR039W, YJL109C, YPL012W, YGR103W, YLR449W, YOR206W, YKL014C, YLL008W, YKL172W, YNL002C, YLR002C, YGL111W, YOL041C, YGL019W, YOR145C, YPR016C	
3	5.417	12,65	YGL011C, YOL038W, YPR103W, YMR314W, YBL041W, YOR362C, YER012W, YJL001W, YML092C, YGR253C, YER094C, YGR135W	
4	5	15,75	YPL043W, YMR290C, YER006W, YKR081C, YDR496C, YDL031W, YNL061W, YNL132W, YLR222C, YLR197W, YMR049C, YHR052W, YJL069C, YKL099C, YDL014W	
5	5	12,60	YPR187W, YPR010C, YPR110C, YNL248C, YOR341W, YNR003C, YKL144C, YOR207C, YPR190C, YNL113W, YOR116C, YBR154C	

☐ Create a new child network.

Plugins

- BiNGO

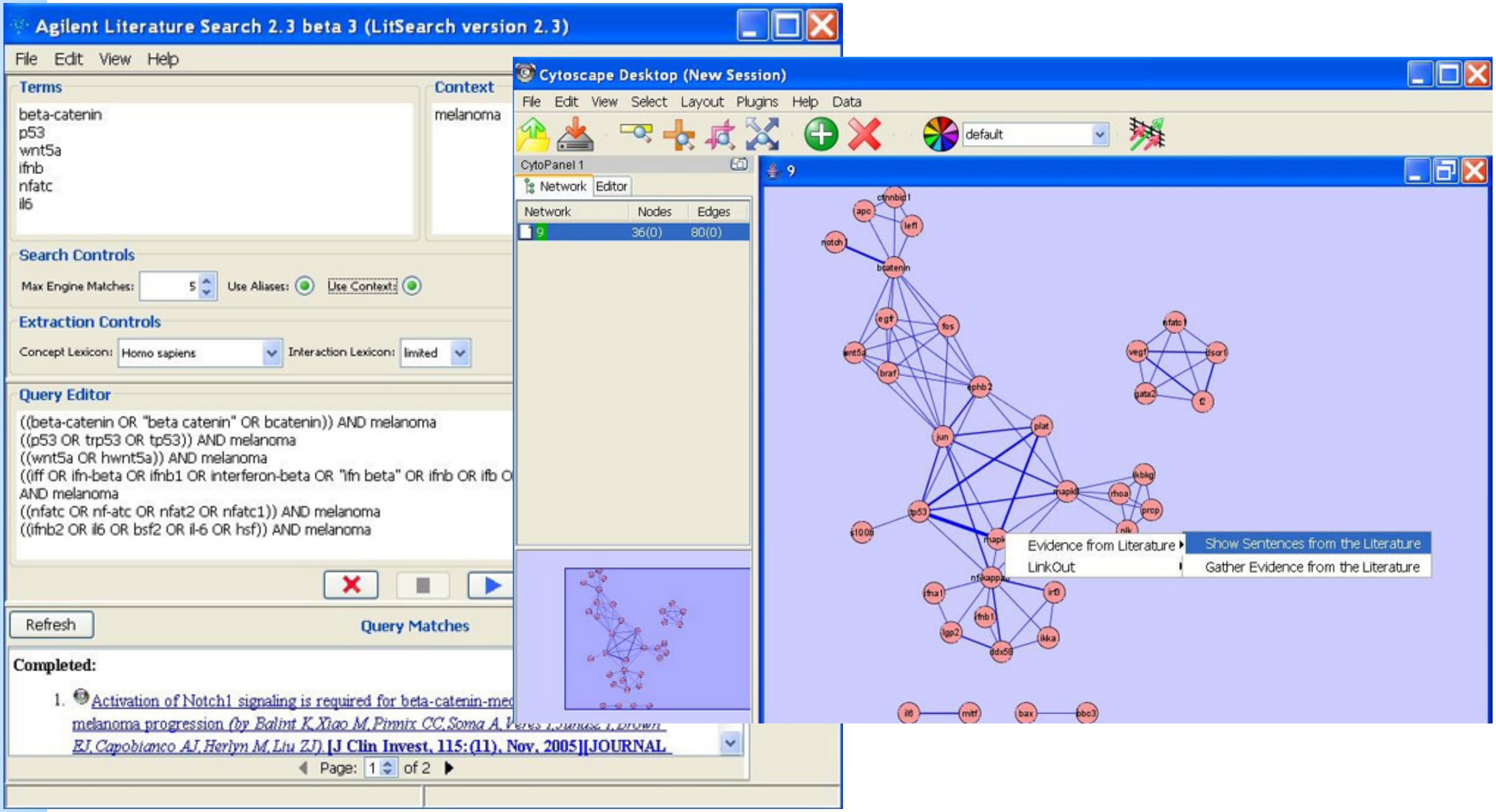


Network	Nodes	Edges
C:\Program Files\Cy	331(25)	362(40)
test	99(0)	135(0)
test2	17(1)	17(0)

Welcome to Cytoscape 2.3 Right-click + drag to ZOOM Middle-click + drag to PAN

Plugins

- Agilent Literature Search



Terms:
beta-catenin
p53
wnt5a
ifnb
nfatc
il6

Context: melanoma

Max Engine Matches: 5 Use Aliases: ● Use Context: ●

Concept Lexicon: Homo sapiens Interaction Lexicon: limited

((beta-catenin OR "beta catenin" OR bcatenin)) AND melanoma
((p53 OR trp53 OR tp53)) AND melanoma
((wnt5a OR hwnt5a)) AND melanoma
((iff OR ifn-beta OR ifnb1 OR interferon-beta OR "ifn beta" OR ifnb OR ifb O
AND melanoma
((nfatc OR nf-atc OR nfat2 OR nfatc1)) AND melanoma
((ifnb2 OR il6 OR bsf2 OR il-6 OR hsf)) AND melanoma

Completed:

1. Activation of Notch1 signaling is required for beta-catenin-me melanoma progression *(by Balint K, Xiao M, Pinnix CC, Soma A,* *EJ, Capobianco AJ, Herlyn M, Liu ZJ)* **[J Clin Invest, 115:(11), Nov, 2005][JOURNAL**

Page: 1 of 2

Network	Nodes	Edges
9	36(0)	80(0)

Tutorial

- Start with “Introduction to Cytoscape”
  - **NOTE**: When you get to the “WikiPathways” step (page 7), you will need to go to the **Plugin Manager** and load the GPML Plugin (under Network & Attribute I/O)
  - Details on the **Plugin Manager** are available on page 11 of the handout.
- Other available handouts:
  - Agilent Literature Search
  - ClusterMaker
  - Network Analyzer
- Don’t hesitate to ask questions!

After Today

- Downloading cytoscape:
  - – www.cytoscape.org
- Questions about cytoscape
  - – cytoscape-helpdesk@googlegroups.com
  - – cytoscape-discuss@googlegroups.com
- Tutorials web site:
  - – http://labrador.library.ucsf.edu/opentutorials/
  - – http://opentutorials.rbvi.ucsf.edu/ (new URL)
- My contact information:
  - – scooter@cgl.ucsf.edu
  - – http://www.cgl.ucsf.edu/home/scooter
  - – http://www.rbvi.ucsf.edu/cytoscape (documentation on our plugins)

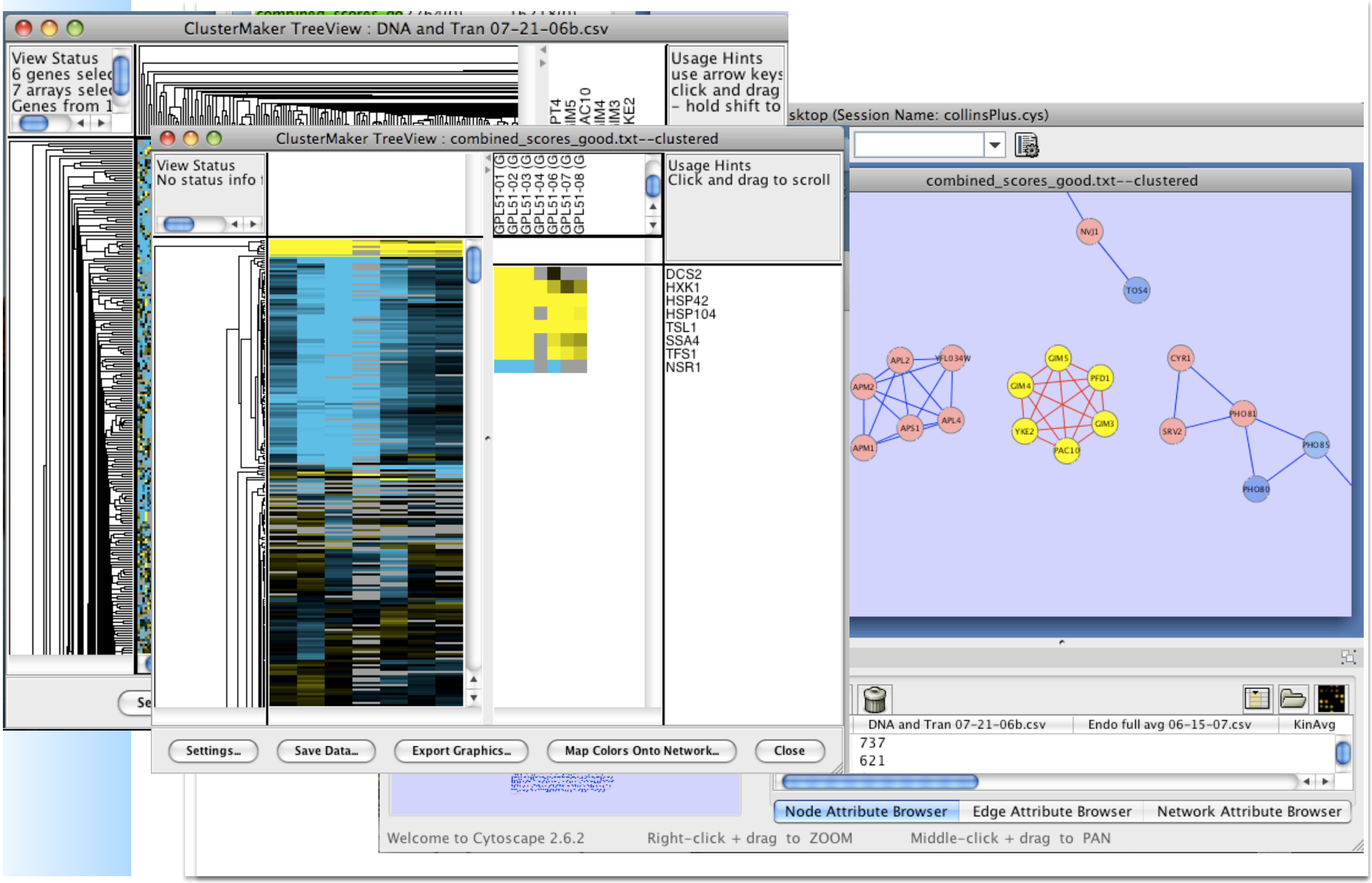
Thanks!

Backup Slides

clusterMaker

- Base Cytoscape:
  - – Map expression values onto network
- Next step: *clusterMaker*
  - – Visualize expression heat maps
  - – Include standard clustering approaches
    - Hierarchical, k-Means
  - – Provide interaction between head map and network
  - – Extensions:
    - epistatic maps, complex determination

clusterMaker



ClusterMaker TreeView : DNA and Tran 07-21-06b.csv

View Status
6 genes selec
7 arrays selec
Genes from 1

Usage Hints
use arrow keys
click and drag
– hold shift to

ClusterMaker TreeView : combined_scores_good.txt--clustered

View Status
No status info

Usage Hints
Click and drag to scroll

DCS2
HXK1
HSP42
HSP104
TSL1
SSA4
TFS1
NSR1

sktop (Session Name: collinsPlus.cys)

combined_scores_good.txt--clustered

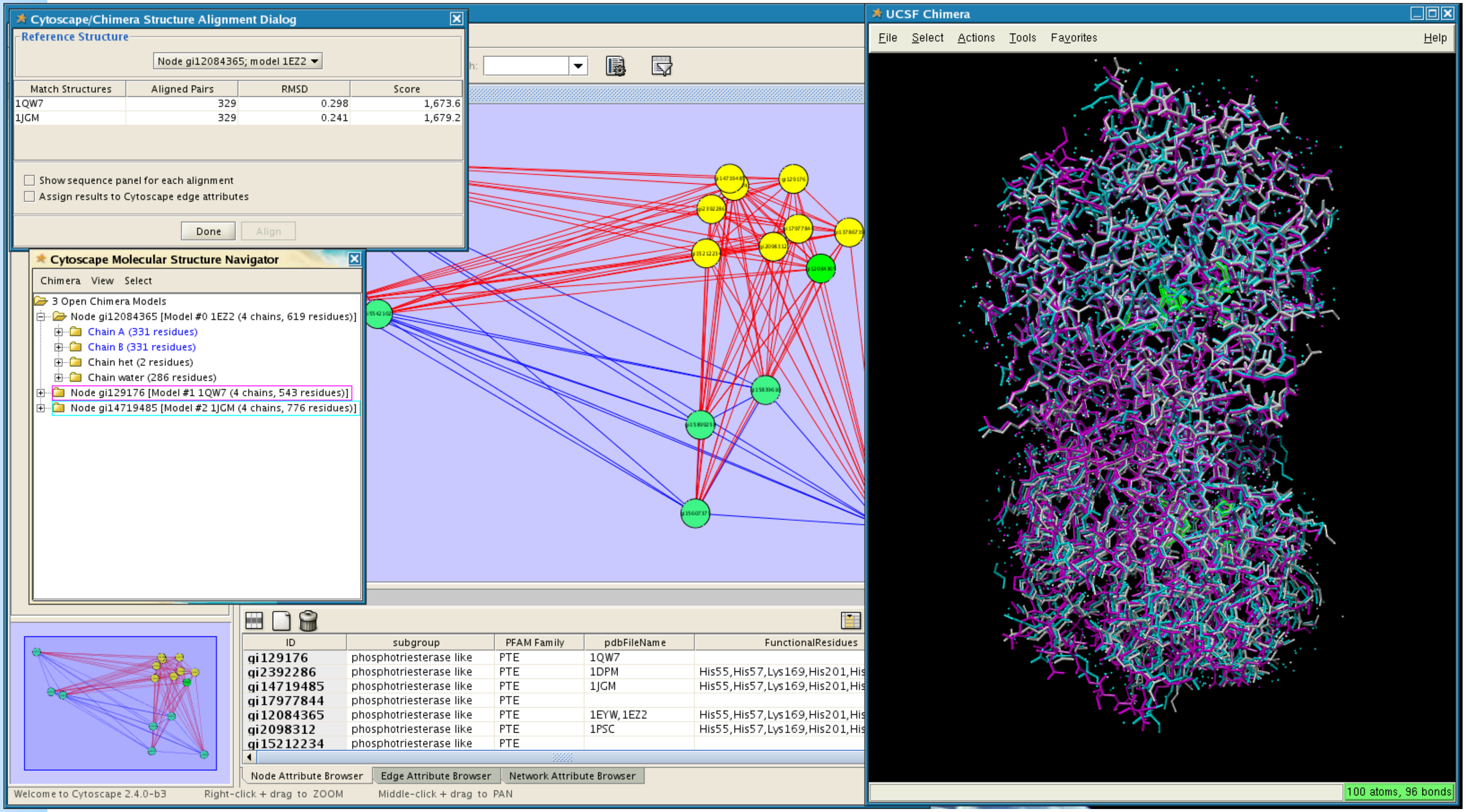
DNA and Tran 07-21-06b.csv	Endo full avg 06-15-07.csv	KinAvg
737		
621		

Welcome to Cytoscape 2.6.2 Right-click + drag to ZOOM Middle-click + drag to PAN

structureViz

- Base Cytoscape:
  - Show protein-protein pathways and interaction networks
- Next step: *structureViz*
  - Use node and edge annotations to provide structural references:
    - PDB files
    - Functional residues
    - Links to modeled structures
  - Visualize structures in UCSF Chimera
    - Provide interaction between structure and network
    - Provide simplified interface to structural elements

structureViz



Node gi12084365; model 1EZ2

Match Structures	Aligned Pairs	RMSD	Score
1QW7	329	0.298	1,673.6
1JGM	329	0.241	1,679.2

☐ Show sequence panel for each alignment
☐ Assign results to Cytoscape edge attributes

3 Open Chimera Models
- Node gi12084365 [Model #0 1EZ2 (4 chains, 619 residues)]
  - Chain A (331 residues)
  - Chain B (331 residues)
  - Chain het (2 residues)
  - Chain water (286 residues)
- Node gi129176 [Model #1 1QW7 (4 chains, 543 residues)]
- Node gi14719485 [Model #2 1JGM (4 chains, 776 residues)]

ID	subgroup	PFAM Family	pdbFileName	FunctionalResidues
gi129176	phosphotriesterase like	PTE	1QW7	
gi2392286	phosphotriesterase like	PTE	1DPM	His55,His57,Lys169,His201,His
gi14719485	phosphotriesterase like	PTE	1JGM	His55,His57,Lys169,His201,His
gi17977844	phosphotriesterase like	PTE		
gi12084365	phosphotriesterase like	PTE	1EYW, 1EZ2	His55,His57,Lys169,His201,His
gi2098312	phosphotriesterase like	PTE	1PSC	His55,His57,Lys169,His201,His
gi15212234	phosphotriesterase like	PTE		

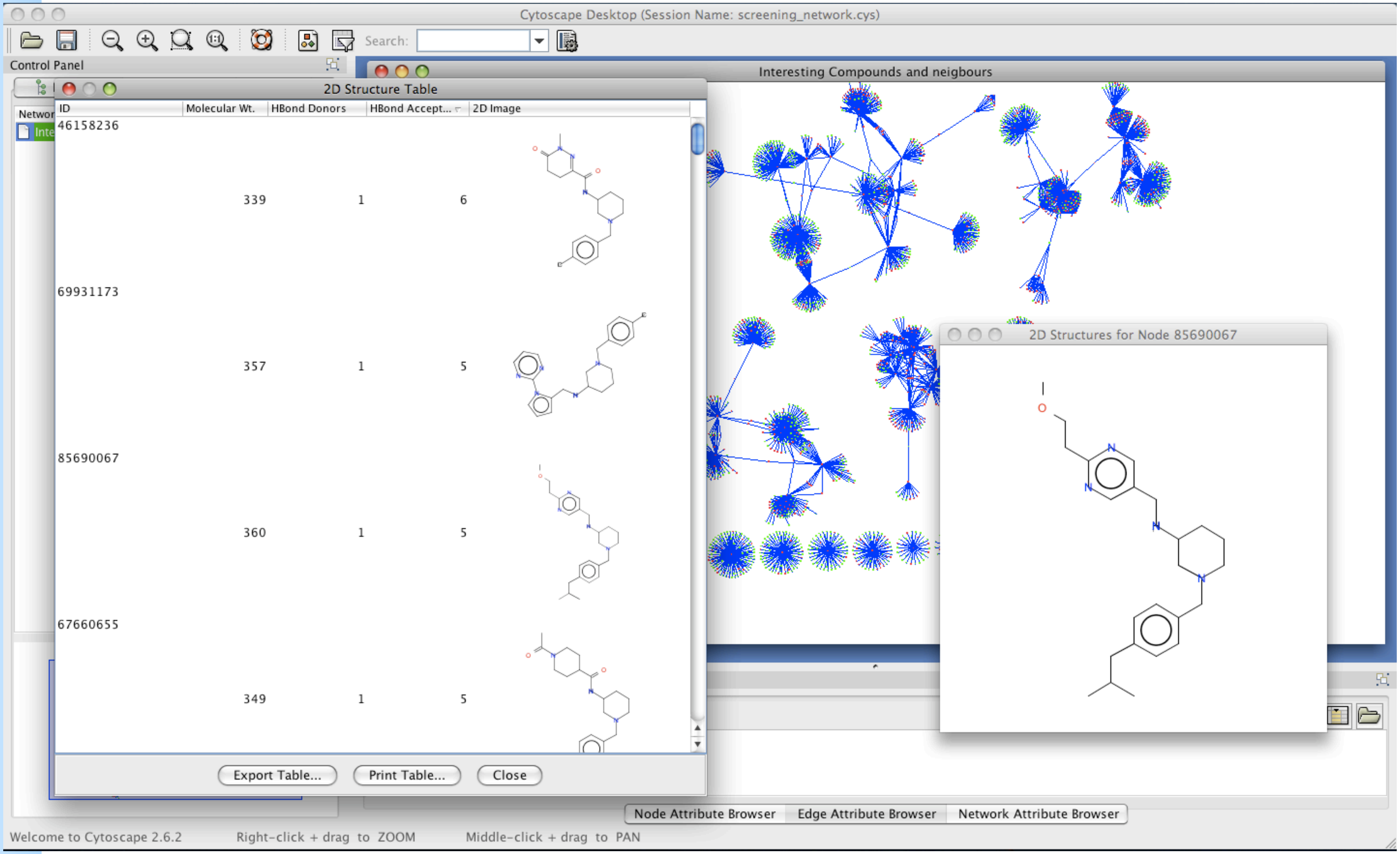
Welcome to Cytoscape 2.4.0-b3 Right-click + drag to ZOOM Middle-click + drag to PAN

100 atoms, 96 bonds

chemViz

- Base Cytoscape:
  - Visualize pathways
    - Color nodes by drug screening results
- Next step: *cheminfo* plugin (*chemViz?)*
  - Use node and edge annotation to provide chemical descriptors
    - SMILES strings, InChi fingerprints
  - Visualize structures
  - Cheminformatics calculations
    - Tanimoto similarity
    - Chemical descriptors (e.g. Rule of Five, Hydrogen Bond Donor and Acceptor count)

chemViz



ID	Molecular Wt.	HBond Donors	HBond Accept...	2D Image
46158236	339	1	6	
69931173	357	1	5	
85690067	360	1	5	
67660655	349	1	5	

Welcome to Cytoscape 2.6.2   Right-click + drag to ZOOM   Middle-click + drag to PAN