

Network2Canvas v1.0 - User Manual

Interacting with the Web Application

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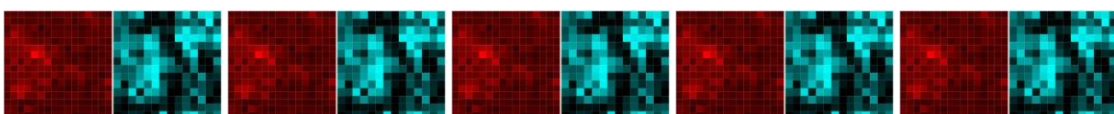
Table of Contents

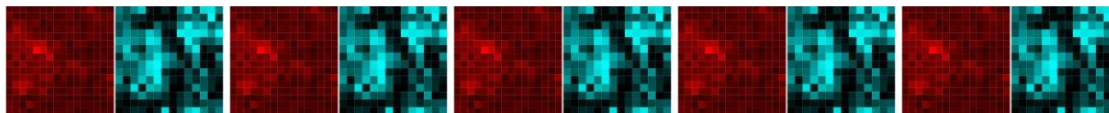
1. Abstract
2. Installation and Requirements
3. N2C User Interface
 - a. The Canvas
 - b. Canvas Options
 - c. Enrichment Analysis
 - d. Download
4. Network2Canvas Learning Game

Abstract

Networks are central in computational systems biology research, but visualizing large networks can be a challenge. For networks larger than ~100 nodes and ~200 links, ball-and-stick diagrams fail to convey much information. To address this, we developed Network2Canvas (N2C), a web application that provides an alternative way to view networks. N2C visualizes network nodes by placing them on a square toroidal grid. These nodes are then clustered together on the grid using simulated annealing to maximize local connections. For visualizing the canvas, a node's brightness is made proportional to its local fitness; the brighter a node is, the stronger its connections to its neighbors. The grid is interactive, implemented in HTML5 and the Java Script library D3.

We applied N2C to create canvases for 25 gene-gene functional association networks connecting human and mouse genes and 6 drug-drug networks connecting FDA approved drugs based on their shared properties. N2C also has functions to perform enrichment analysis which can create unique metasignatures for the input gene list. Given a list of genes or drugs, N2C highlights enriched terms on the grid as well as computes the degree of clustering for these enriched nodes. In summary, N2C provides a new flexible method to visualize large networks and to perform and visualize enrichment analysis on functional drug and gene networks. N2C is freely available at <http://www.maayanlab.net/N2C>.





Installation and Requirements

N2C requires a working internet connection and a modern browser capable of displaying and operating on SVG images. These include FireFox 3.6 or higher, Opera 11.01, Chrome 10, Safari 5, and IE8 or higher versions. You should see this page when pointing your browser to:

<http://www.maayanlab.net/N2C>

Network2Canvas: Network Visualization on a Canvas with Enrichment Analysis

Drug-Drug Similarity Canvases
Functional Association Gene Canvases
Canvas Node-Learning Game

Analysis
Canvas Options

Gene List Enrichment Analysis

Choose Color to Highlight Terms:

Gene List:

Enter list of gene names here

Submit Clear

Example

Find by: Name Element

Find Terms by Name:

Insert Term List (e.g., CDK1 CDK2 CDK3)

Find

[Download Current View in SVG](#)
(Pathway to Adobe Illustrator)

KEGG Pathways

☒ Main View
☐ Network View
☐ P-Value View

Click a spot on the canvas to view more information about the term.

Info
Analysis Output

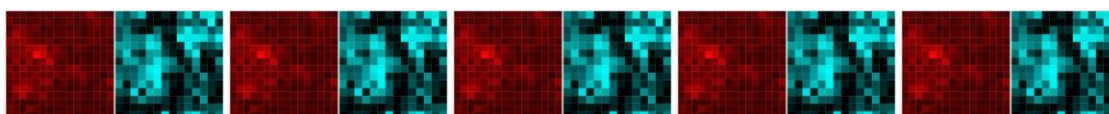
Term Name:

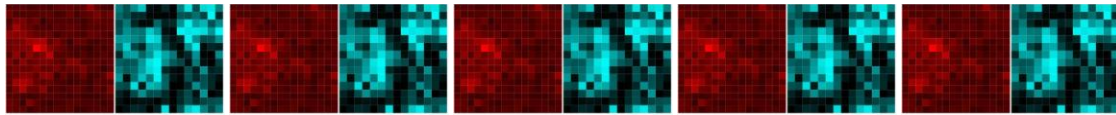
Additional Information:

Add to Input List

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Figure 1: The Network2Canvas Interface.





The N2C User Interface

Network2Canvas: Network Visualization on a Canvas with Enrichment Analysis

Drug-Drug Similarity Canvases

Functional Association Gene Canvases

Canvas Node-Learning Game

Figure 2: Network2Canvas Header. The three hyperlinks link to the drug-drug similarity canvases, the functional association gene canvases, and the canvas node-learning game. These links only appear in the online version of N2C found at <http://www.maayanlab.net/N2C>. If the visualizer page was created using the Network2Canvas script, these links will be replaced by "Offline N2C."

Interacting with the Canvas

The canvas object has a zoom-in feature that is accessed through the mouse wheel. It also supports panning. When the mouse pointer hovers over a node, the name of the node will be shown next to the pointer. Clicking on a node will bring up a list of genes associated with that node underneath the Info tab.

The dropdown box allows you to choose the various canvases. The offline version's dropdown box is disabled, and the name of the canvas is the filepath of the matrix used to create the canvas with the N2C Annealer.

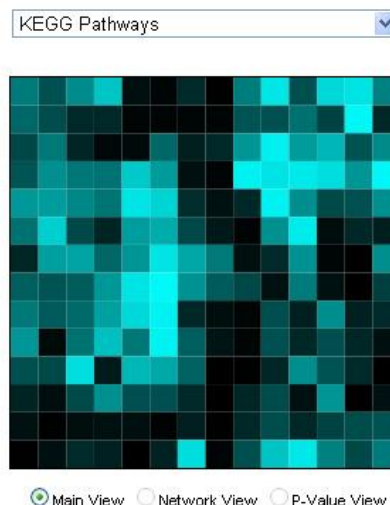
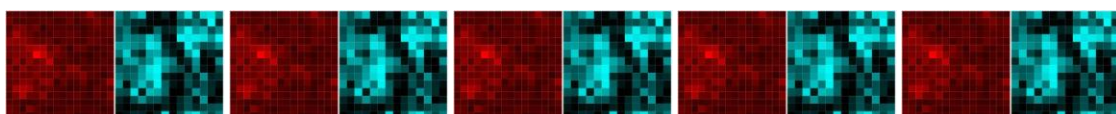
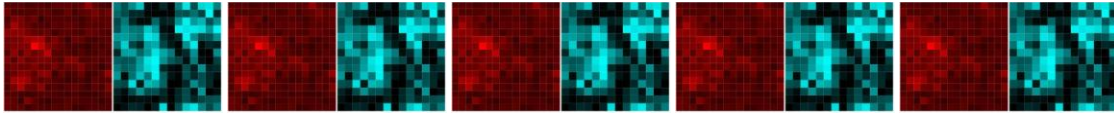


Figure 3: The canvas object in N2C. The dropdown box displays the file path of the matrix used to create the canvas. The canvas object currently displays the main view, a grid of nodes where each node's brightness is proportional to the similarity to its neighbors. Enrichment analysis enables viewing the other two views.





Canvas Options

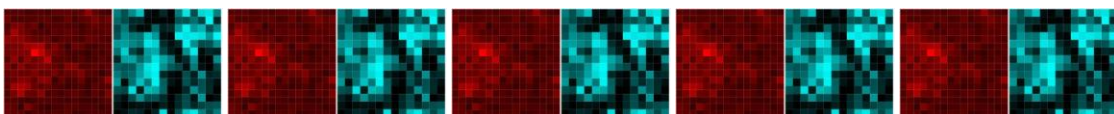
The canvas options tab allows you to change the properties of the canvas object. The colors can be changed by selecting the color on the color wheel.

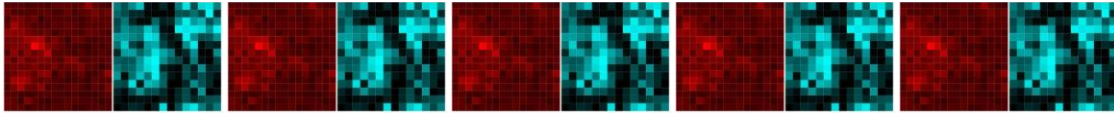
A color scale feature allows you to adjust the colors of the canvas to provide greater contrast between similarly colored nodes.

The Center Canvas button allows you to reset the canvas position back to default.



Figure 4: Canvas Options. Network2Canvas allows the user to change the color of the canvas and to adjust the color scaling to give better contrast between similarly-colored nodes.





Find Term/Element Feature

Specific terms in the gene set library of the canvas can be found by using the ***Find by Term*** function. After submitting a list of terms, the list of terms will be highlighted on the canvas.

Additionally, the ***Find by Function*** has an option to search gene set library terms by submitting genes that are associated with it. Any term with the gene in its list will be lit on the canvas. This function is different from Gene List Enrichment Analysis.

Find by: Name Element

Find Terms by Name:

Insert Term List
 (e.g.,
 CDK1
 CDK2
 CDK3)

Find

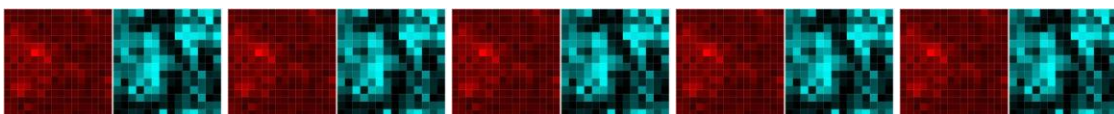
Find by: Name Element

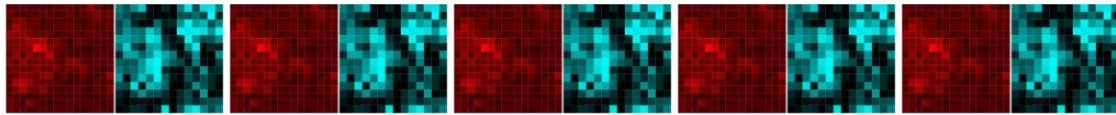
Find Terms by Element(s):

Insert Element
 List (e.g.,
 CDK1
 CDK2
 CDK3)

Find

Figure 5: The find function. Find by Name identifies all nodes that share a name with the list of inputted terms. Find by Elements identifies all nodes that contain an element from the input list based on the GMT File associated with the canvas.





Gene List Enrichment Analysis

Enrichment analysis can be performed under the Analysis Tab. By adding a list of genes and choosing the color of the indicating marks (default is white), Network2Canvas runs enrichment analysis using the GMT file associated with the canvas. The p-values of the top 20 enriched terms will display under the Analysis Output tab. These p-values are computed using the Fisher exact test.

Significant enriched terms will be highlighted on the canvas in the chosen color. Two other views are also produced from the enrichment analysis.

The network view connects the enriched terms through their nearest neighbor distance while the p-value canvas view highlights the top 20 squares with the chosen color; the brightness of the chosen color corresponds to the node's significance score ($1 - p\text{-value}$).

A download link is provided underneath the canvas which shows all the significant enriched terms, their p-values, and a list of intersecting genes.

Analysis

Canvas Options

Gene List Enrichment Analysis

Choose Color to Highlight Terms:

Gene List:

NFATC2

GALNT7

SESN1

NMUR1

ACYP2

IL12RB1

Submit

Clear

KEGG Pathways

Main View

Network View

P-Value View

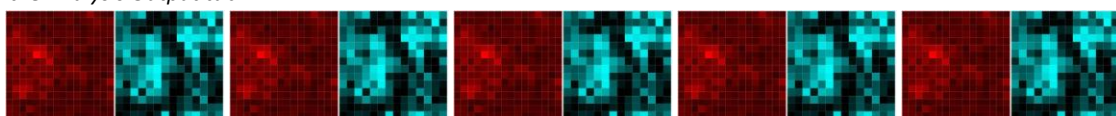
Click a spot on the canvas to view more information about the term.

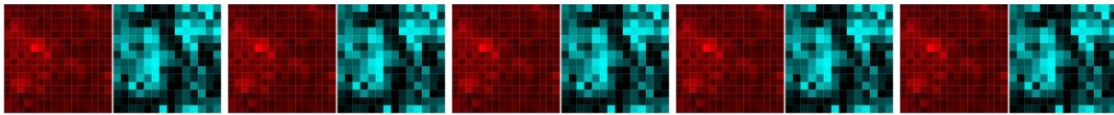
Info

Analysis Output

Term	P-Value
HSA00760_NI COTINATE_A ND_NICOTIN AMIDE_MET ABOLISM	5.886e-2
HSA00910_NI TROGEN_ME TABOLISM	5.886e-2
HSA00632_B ENZOATE_D EGRADATIO N_VIA_COA_ LIGATION	6.798e-2
HSA00512_O _GLYCAN_BI OSYNTHESIS	7.477e-2
HSA00620_P YRUVATE_M ETABOLISM	9.929e-2
HSA04662_B _CELL_RECE PTOR_SIGNA LING_PATHW	1.466e-1

Figure 6: Enrichment Analysis. For Gene List Enrichment Analysis, the gene list is submitted into the visualizer. Afterwards, using the GMT file associated with the canvas, enrichment analysis is performed and the top 20 results are outputted on the canvas and on the Analysis Output tab.





Download Canvases and Networks

The download canvas link can be found on the bottom left corner of the N2C Page. Clicking the link will allow you to download the current active canvas in SVG format.

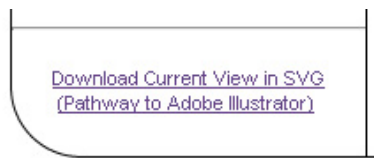
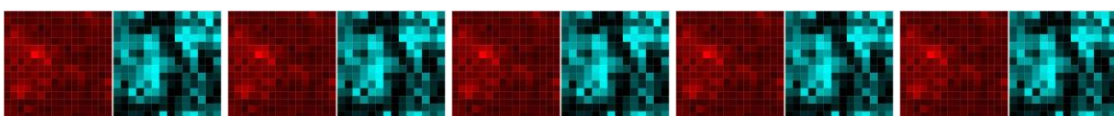
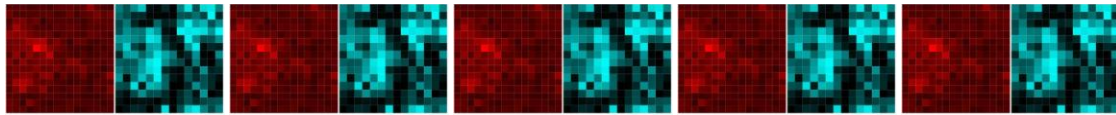


Figure 7: Current SVG View Download. This link allows downloading of the current canvas view.





Network2Canvas Learning Game

Choose Level

1. Choose Level:

Level 2 - Medium

Scoreboard

Name	Score
Avi	17557
Avi	16498
Avi	15283
Avi	14219
Yan	13798
Chris	10336
rb	9175
Yan	8340
John	6293
Yan	4849

Canvas: PFAM Interpro - Protein Domains

Points: -1200 Nodes Left: 10

Time: 18 Clicks Left: 78

Please Find : GCN5ACETYL_TRANS

About Find

Find Terms

GCN5ACETYL_TRANS

DNA_POL_BETA

PPIASE_FKBP

RASGRF_CDC25

POU_SPECIFIC

LECTIN_C

PPIASE_CYCLOPHILIN

CYCLIN_N

DEAD/DEAH_N

SCP-LIKE_EXTRACELLULAR

Figure 8: Network2Canvas Learning Game Interface.

How to Start the Game

1. Choose your level: Easy, Medium, Hard, Master
2. Choose your canvas
3. Press the Start button

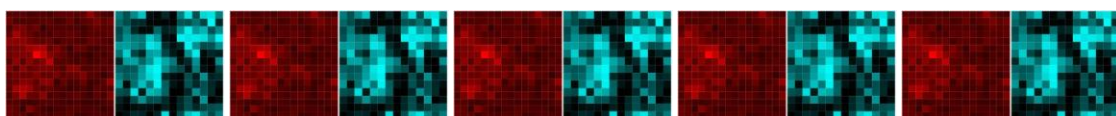
How to Play the Game

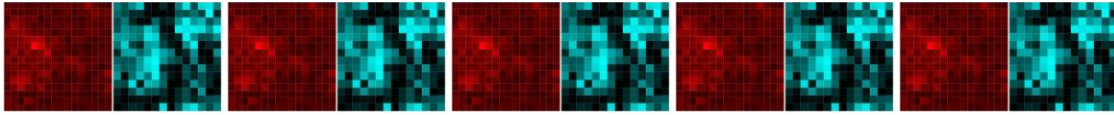
After starting the game, the entire canvas will be blacked out, and the names of ten nodes will appear in the Find tab. The node to find will appear in red text. Clicking on the canvas will reveal one of three colors: red, blue, and white.

The brighter the red, the closer you are to the node. The brighter the blue, the further away you are from the node. White means you correctly chose the node.

After you selected the correct node, all the wrong nodes you selected become black, and the name on the list will turn green. You will be instructed to find the next node on the list.

The game ends when you click 100 wrong nodes or find all 10 nodes on the list.





Scoring

Points are awarded based on the following:

- How fast you find the nodes
- How many clicks you have remaining after finding all the nodes on the list
- The size of the canvas you played the game on

Points are penalized based on the following:

- Wrong clicks subtract points from your score

Submitting Your Score

After finishing the game, you have the option to submit your score to the scoreboard.

