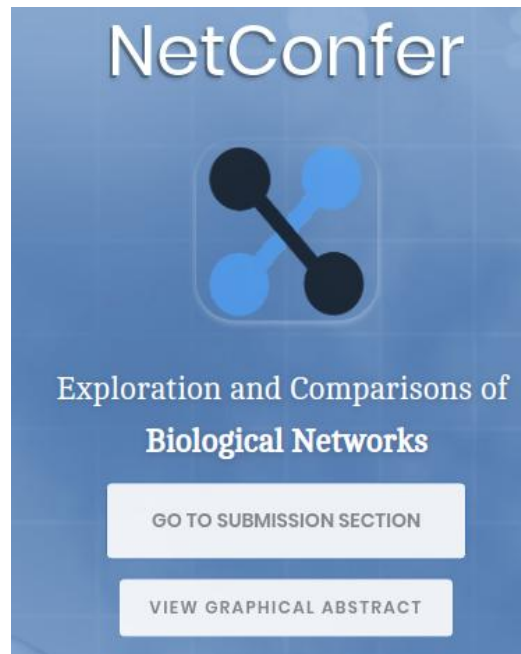


NetConfer User manual

NetConfer is a web based tool designed for comparative analysis of multiple interaction networks. It implements various analysis methods organized as workflows. It must be noted that NetConfer is not a network visualization tool and it intends to assist various comparative analysis using interactive visualizations. To start the tutorial, please visit the NetConfer web-page (web.rniapps.net/netconfer) and click on the button 'Go to submission section'.

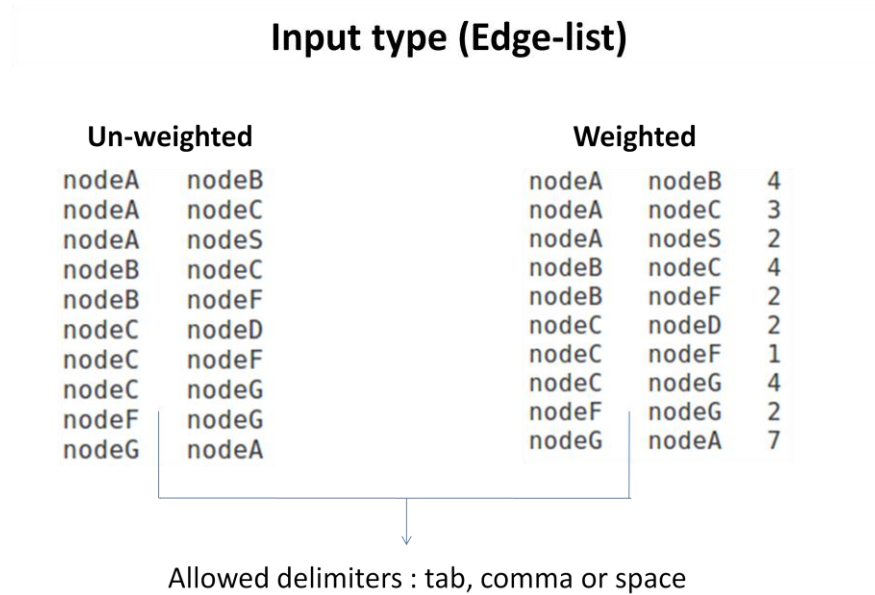


In order to demonstrate the features, we will use a tutorial with five simple networks available as Example 1 (simple generic example). This example can either be auto-loaded by clicking the 'Execute demo' button or by downloading the individual files (by clicking 'details') and uploading the same.

The image is a screenshot of the NetConfer interface for "Example 1: Simple Generic Example". The interface has a dark blue header with the example title. Below the header, there are two buttons: "Execute Demo" (blue) and "details" (grey). Underneath these buttons, there is a reference text: "Ref. General example for ease of understanding the platform". To the right of the interface, there is a text block explaining that five simplified hypothetical networks are created to demonstrate the utilities of CrossNet, and that these are tab-separated edge lists representing five different weighted networks. Below this text, there are five buttons labeled "Net1", "Net2", "Net3", "Net4", and "Net5", each in a different color (blue, grey, blue, grey, blue).

Data input

Users can upload a set of networks into NetConfer either as an edge-list (tab/space/comma delimited)



The tutorial example is a tab delimited edge-list file with equally weighted edges. Hence if a user chooses to run the examples after uploading the files, the file format should be selected as 'EDGE LIST', Delimiter as 'tab' and Weighted as 'Yes'. The uploaded networks are automatically assigned a color and a label which can be edited as per user convenience. The tool also has provisions to append additional networks to an existing set.

The screenshot displays the 'Submission Steps' interface for NetConfer. It consists of four numbered steps:

- Step 1: Specify De-limiter**: Shows radio buttons for 'Tab' (selected), 'Comma', and 'Space'.
- Step 2: Specify weight**: Shows radio buttons for 'Weighted' and 'Unweighted'.
- Step 3: Assign Recognizable Job Label**: A text input field containing 'test label'.
- Step 4: Finally, Upload Upto 8 Edge Lists**: Includes a 'Browse...' button, the text 'No files selected.', and an 'Upload' button.

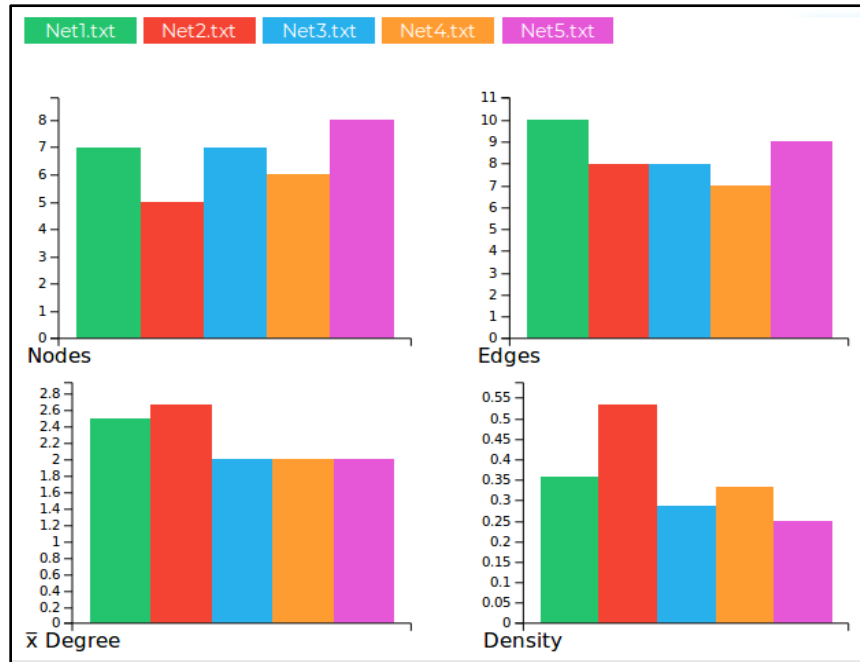
To the right, there is a 'Change labels and color (optional)' section with five color swatches labeled 'Net1.txt' through 'Net5.txt'. A color selection tool is open, showing a color gradient and a hex code input field containing '#ff9c31'.

At the bottom right, a 'STATUS TERMINAL' window shows the following output:

```
STATUS TERMINAL
test label is job label
Specified Unweighted network
Tab chosen as delimiter
```

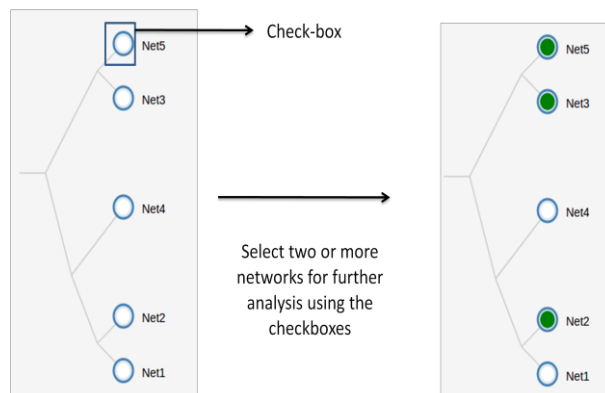
Network dashboard

The global properties namely total node, total edge, cluster coefficient and network density are calculated for each uploaded network and presented as faceted bar plots. This allows the user to get an initial idea of the network structures and proceed for further analysis using the 'Proceed' button.



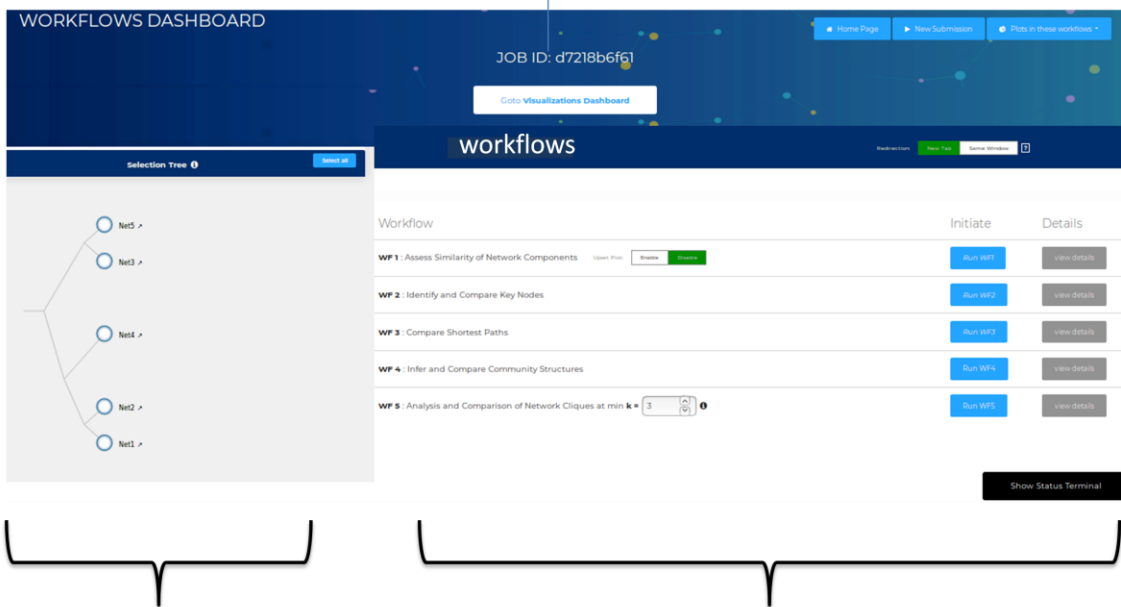
The following page presents a pre-clustered view of the input networks based on their edge similarity (calculated using a Jaccard index) in the form of a tree. The nodes of the tree can be clicked to confirm analysis on a selected set of networks based on user's choice.

Networks auto clustered based on their similarity (Edge-Jaccard score) for ease of selection



NetConfer allows users to perform analysis either using the 'workflows dashboard' or 'visualization dashboard'. As the name implies, each workflow (in the 'workflow dashboard') is intended to enable the end user accomplish a specific analysis objective whose output is presented as user friendly visualizations. The uploaded networks are automatically clustered based on their overall similarity (based on Edge Jaccard Index) and presented to the user for ease of selection. Each workflow can then be applied over a user selected set of networks for further analysis. Various workflows focus on comparative analysis of nodes, edges, graph properties, shortest paths, community structures and network cliques. A unique job ID is assigned for every user run which can be tracked from the option 'Access previous jobs'.

Unique JOB ID for every user run



Select a set of networks Apply an analysis workflow on the selection

The visualization dashboard on the other hand, allow users to perform more visualization focused analysis on the selected networks like viewing union, intersection and exclusive parts of selected networks, network property mapping visualization and view distance of individual networks from the global union network.

VISUALIZATION DASHBOARD

JOB ID: 5890630d18

Go to Workflows Dashboard

Visualization modules

Selection Tree

Module	Initiate	Details
Module 1 : Intersection Visualization	Run Module 1	View details
Module 2 : Exclusives Visualization	Run Module 2	View details
Module 3 : Union Visualization	Run Module 3	View details
Module 4 : Property Mapped Individual Networks	Run Module 4	View details
Module 5 : Distance from the Union	Run Module 5	View details

Description of NetConfer Workflows

1. **Assess similarity of network components:** This workflow identifies nodes/edges which are commonly shared or exclusive to one or more of the selected set of networks. It uses a powerful visualization technique called 'upset plot' augmented with interactive user operations to graphically display the similarities and differences.
2. **Identify and compare key nodes:** This workflow allows identification and comparison of key nodes between selected networks using local graph property measures. For an ordered selection, a 'delta centrality' calculation is made to identify discriminating nodes and displayed using parallel coordinates.
3. **Compare shortest paths:** This workflow allows performing a comparative analysis of shortest paths between a given pair of nodes across a selected set of networks. The output is presented graphically for identification of critical nodes in information flow.
4. **Infer and compare community structures:** This workflow is designed to identify and capture changes in community structure (densely connected group of nodes) across the selection. A 'sanky plot' is used to represent changes in community between a set of selected networks.
5. **Analysis and comparison of network cliques:** This workflow is designed to find and compare 'cliques' (closely knit subset of nodes in a graph) between networks. Cliques can be useful in several biological systems like identification of co-expressed genes, finding (and comparing) motifs or analyzing microbial communities.

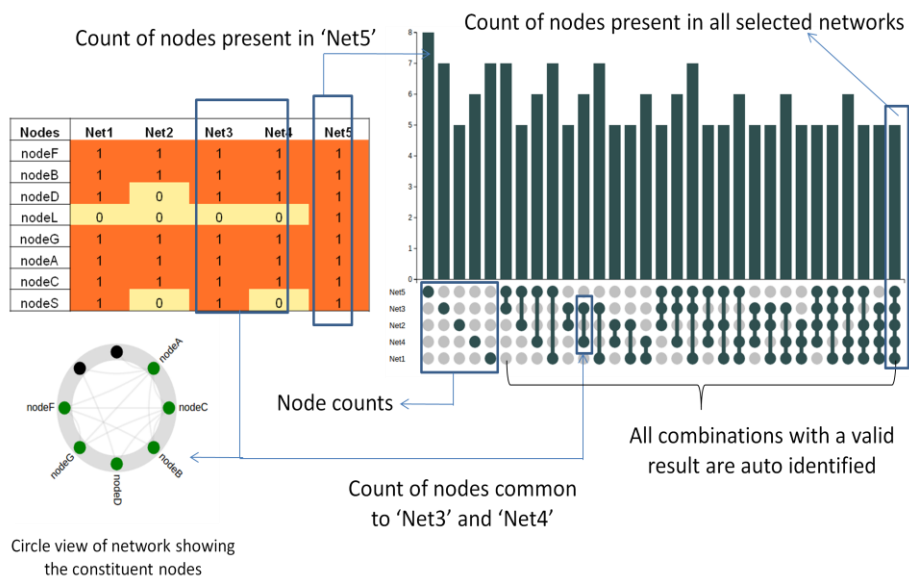
NetConfer Workflow 1

Assess Similarity of Network Components

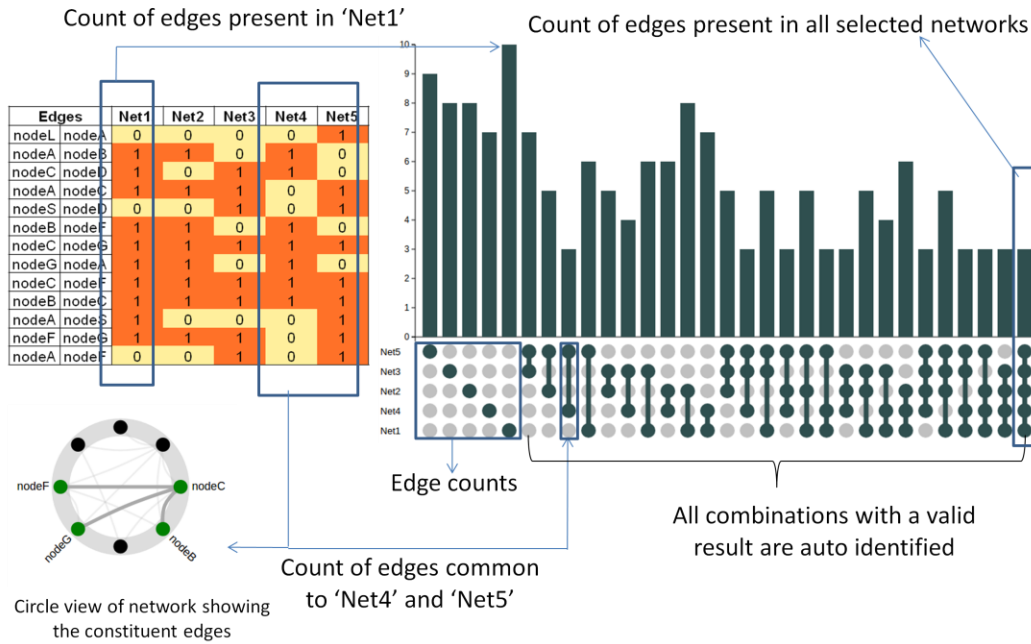
Objective: This workflow helps users compare the similarity of the node and edge composition of several networks simultaneously. The output of the workflow is an interactive visualization composed of an Upset Plot (with Circular Graph) and Venn diagrams.

Interpretation: The UpSet technique visualizes set intersections (in this case, common nodes or edges among different networks) in a matrix layout and introduces aggregates based on groupings and queries. The matrix layout enables the effective representation of associated data, such as the number of elements in the aggregates and intersections. Users have the choice of finding both the common nodes and the common edges between the selected networks. Clicking on a bar also shows the network components in a circular graph.

Interpretation of the UpSet plot (Nodes)

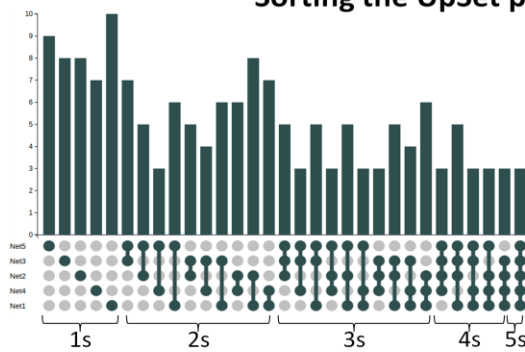


Interpretation of the UpSet plot (Edges)



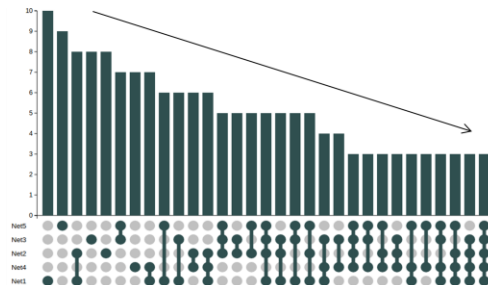
The bars in the UpSet plot can be sorted either based on the cardinality (ones, two's, three's, etc.) of the combinations or the set size of a combination set as shown below :

Sorting the UpSet plots



Combination Cardinality

Plot bars sorted by the size of the combinations

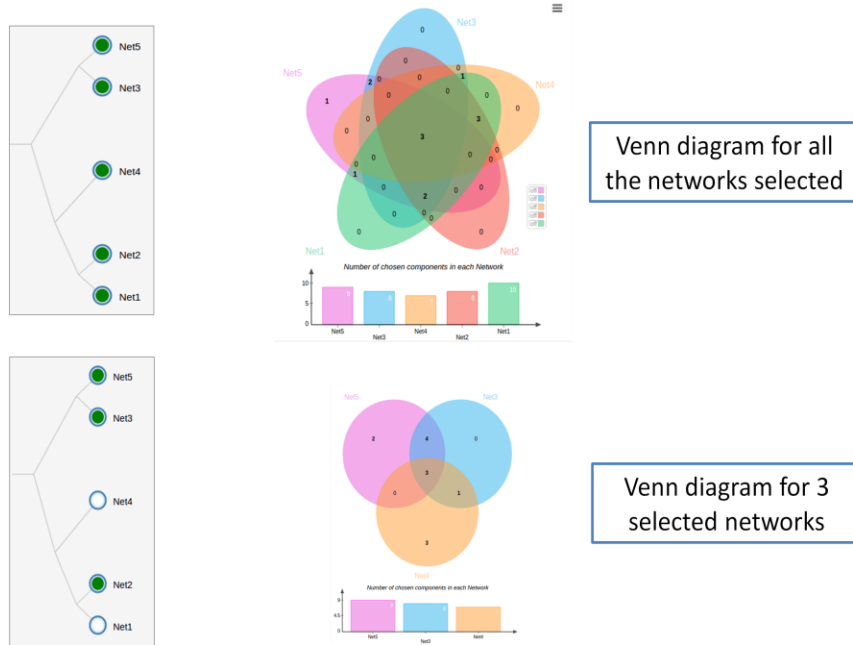


Set Cardinality

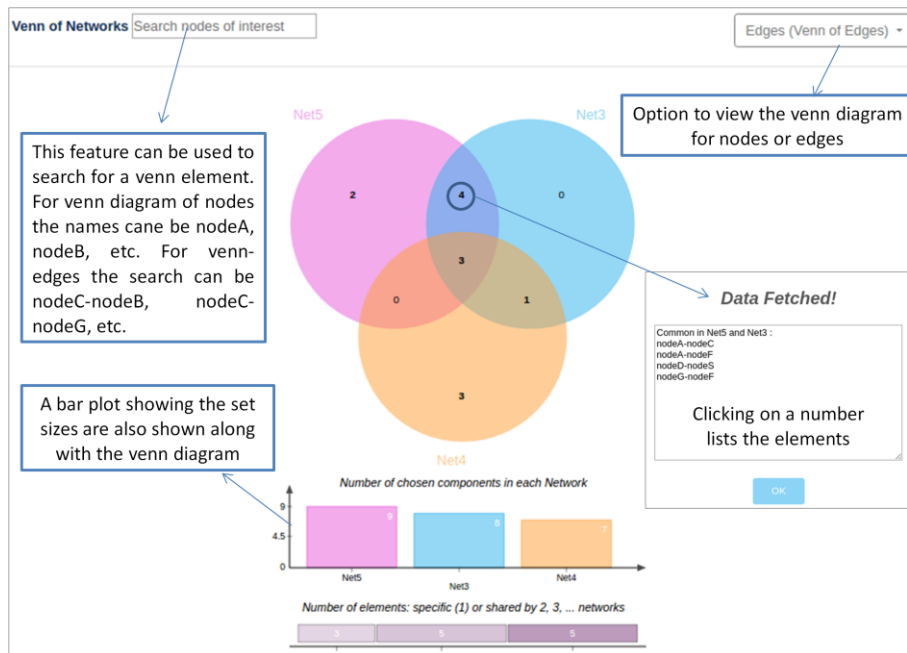
Plot bars sorted by the size of the sets

NetConfer also allows visualizing the network components (nodes/edges) using venn diagrams. However, venn diagrams are restricted to view upto six networks at a time.

Generating venn diagrams based on user selection



Visualize network components using venn diagrams



NetConfer Workflow 2

Identify and Compare Key Nodes

Objective: This workflow helps users identify and compare key nodes. There are three basic outputs of this module:

1. Global property of the networks: Allows to assess and compare the global network structure.
2. Table of the local properties of various nodes across different networks: Allow understanding the importance of each node with respect to a network.
3. Delta centrality viewer: Comparison of network properties of each node and visualize its change across the selected networks.

Interpretation:

The global properties viz. average clustering coefficient, average shortest distance, density, diameter, number of edges and number of nodes are presented as sortable tabulated outputs. Users also have the option to download the table as a CSV File.

The screenshot shows a web interface with a navigation bar at the top containing 'About', 'Nodes across networks', 'Local Properties of Nodes', and 'ΔCentrality Measures'. Below the navigation bar is a 'WELCOME' section with a paragraph explaining the workflow's purpose. A text block below that states: 'Following is an overview of the global properties of various networks chosen by you for this workflow.' To the right of this text is a blue 'Export Table' button. Below the text is a table with the following data:

Graph	Total Nodes	Total Edges	Diameter	Density	Clust Coefficient	Avg Degree
Net1	7	10	3	0.357143	0.48	2.5
Net2	5	8	2	0.533333	0.666667	2.66667
Net3	7	8	3	0.285714	0.375	2
Net4	6	7	3	0.333333	0.25	2
Net5	8	9	4	0.25	0.352941	2

At the bottom of the table, there is a pagination bar with buttons for 'First', 'Prev', '1', 'Next', and 'Last'.

Some of the most useful (local) properties of nodes in a network covered by NetConfer are degree, betweenness centrality, hub and authority score, eccentricity and eigenvector centrality. The workflow allows tabulated and graphical analysis and tracing of various properties across

selected set of networks. These properties can be viewed by sortable and searchable tables for comparing the node properties across different networks. Further the table can be generated by either having the values of one of the properties of a node across different networks or having the different properties of all the nodes in one network. The first option is useful for understanding the changes in centrality measure across different networks.

Nodes across networks

Betweenness
 Degree
 Closeness
 HubScore
 Eigenvector
 [Export Table](#)

Nodes	Net5	Net3	Net4	Net2	Net1
nodeA	14.0	0.0	0.5	0.333	5.333
nodeC	8.0	11.5	5.5	0.667	6.0
nodeS	6.0	0.0	-1.0	-1.0	0.0
nodeF	2.0	0.5	0.0	0.333	0.333
nodeB	0.0	0.0	2.0	0.333	0.667
nodeG	0.0	0.0	1.0	0.333	0.667

[First](#)
[Prev](#)
[1](#)
[2](#)
[Next](#)
[Last](#)

Networks across nodes

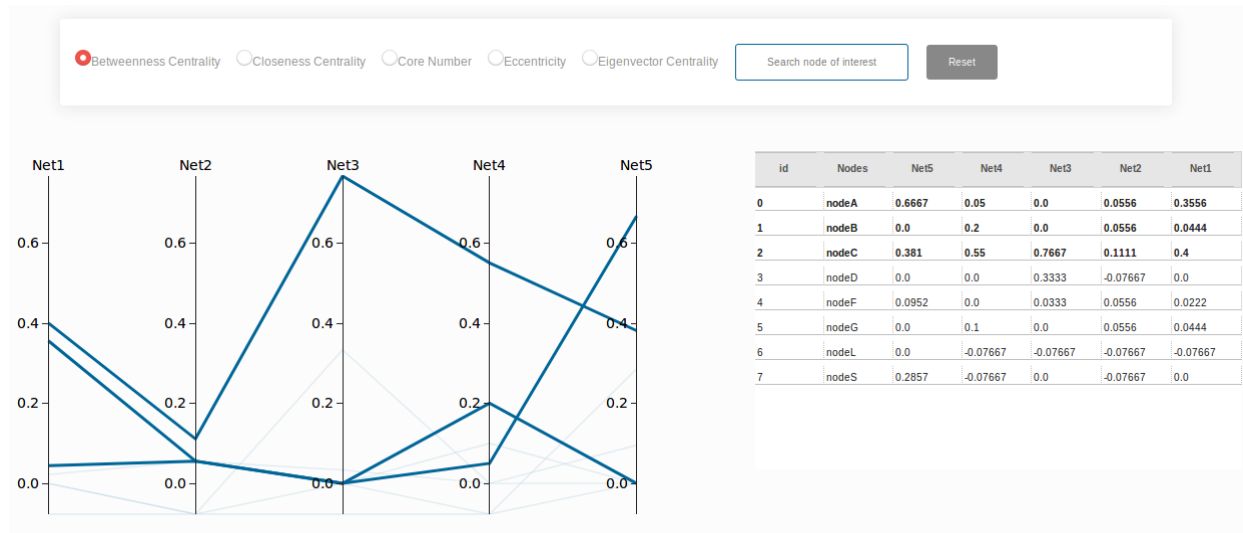
Net5
 Net3
 Net4
 Net2
 Net1
 [Export Table](#)

Node	Degree	Closene...	Betwee...	EigenVe...	Network...	Clustering...	PageRank	HubScore	Authority...
nodeA	4.0	0.7	14.0	0.489	0.375	0.167	0.111	0.806	0.0
nodeC	4.0	0.636	8.0	0.536	0.484	0.333	0.142	0.498	0.542
nodeS	2.0	0.5	6.0	0.196	0.547	0.0	0.091	0.0	0.405
nodeF	3.0	0.583	2.0	0.487	0.708	0.667	0.151	0.168	0.655
nodeB	1.0	0.412	0.0	0.188	1.188	0.0	0.06	0.273	0.0
nodeG	2.0	0.438	0.0	0.359	0.936	1.0	0.249	0.0	0.335

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The centrality measures of various nodes in a network allow identifying critical or key nodes in a network. For example, in a microbial association network, degree and betweenness might be useful to identify key nodes ('microbes') that help in microbial communication. Nodes with high betweenness score are essentially key points of information flow and if removed can disrupt the whole network. Similarly, hub and authority scores have been proven to be useful in identification of essential proteins in protein-protein interaction networks.

Delta centrality viewer



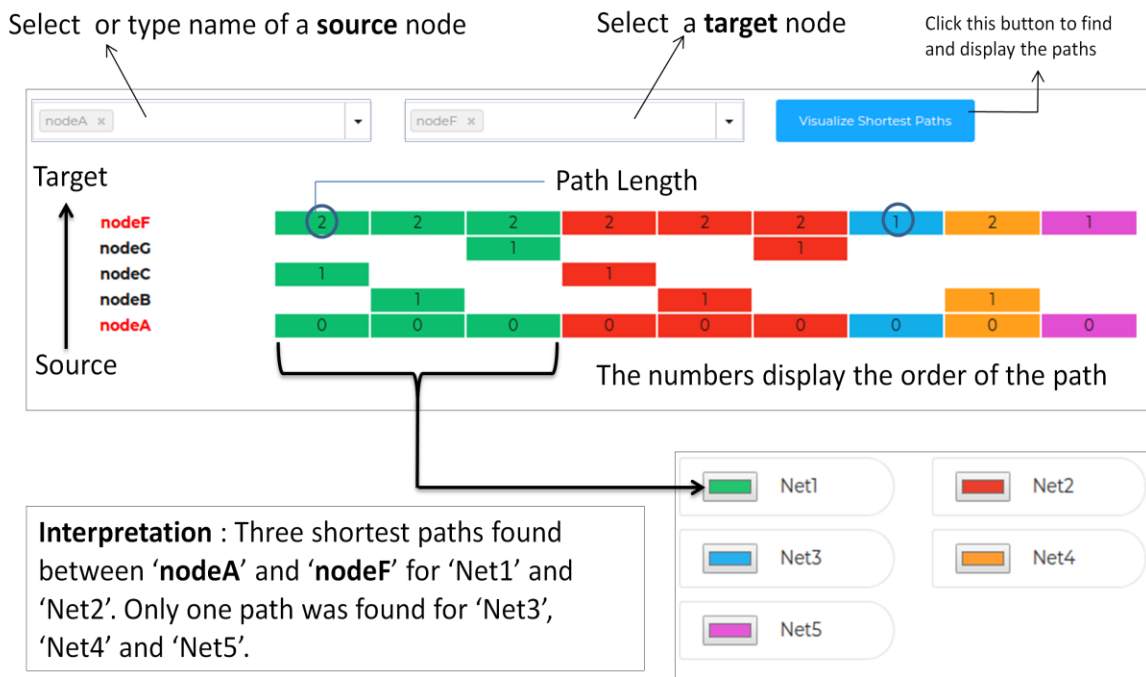
NetConfer provides an innovative solution to view changes in the various centralities utilizing interactive parallel coordinates. In such plot, user can choose a centrality measure using the radio button and highlight the values for one or more selected node using the tabulated summary by clicking on the desired node name. A node can also be searched using the 'Search node of interest' feature. Each axis of the parallel coordinate are scaled to the global max and global min of the observed centrality values for a meaningful interpretation. The axes can be clicked and dragged to reorder the network arrangements. This feature is useful especially for comparing ordered networks (e.g. networks arising from time series data). **N.B:** In order to enable the implementation of the parallel coordinates (which requires a value for each node in each axes), nodes absent in a particular network (represented by the axes) are assigned negative values (to distinguish them from the ones that are present and having a positive value).

NetConfer Workflow 3

Compare Shortest Paths

Objective: This workflow allows performing a comparative analysis of shortest paths between a given pair of nodes across a selected set of networks. The output is presented graphically for identification of critical nodes in information flow.

Interpretation: Users can select a 'source' and 'target' node from the respective dropdowns (or by entering the names manually). After that, clicking the 'Visualize shortest path' button finds and graphically displays the shortest paths. The interpretation of the plot is presented below:



Shortest path identification finds important application in network biology ranging from metabolic pathway analysis, alterations in protein-protein interaction networks, order of interaction cascades in transcription factor networks, etc. NetConfer not only allows comparing multiple shortest paths within a network but also across a selected set of networks in an easy and intuitive way. The outputs of an analysis can also be exported as text files for further analysis.

NetConfer Workflow 4

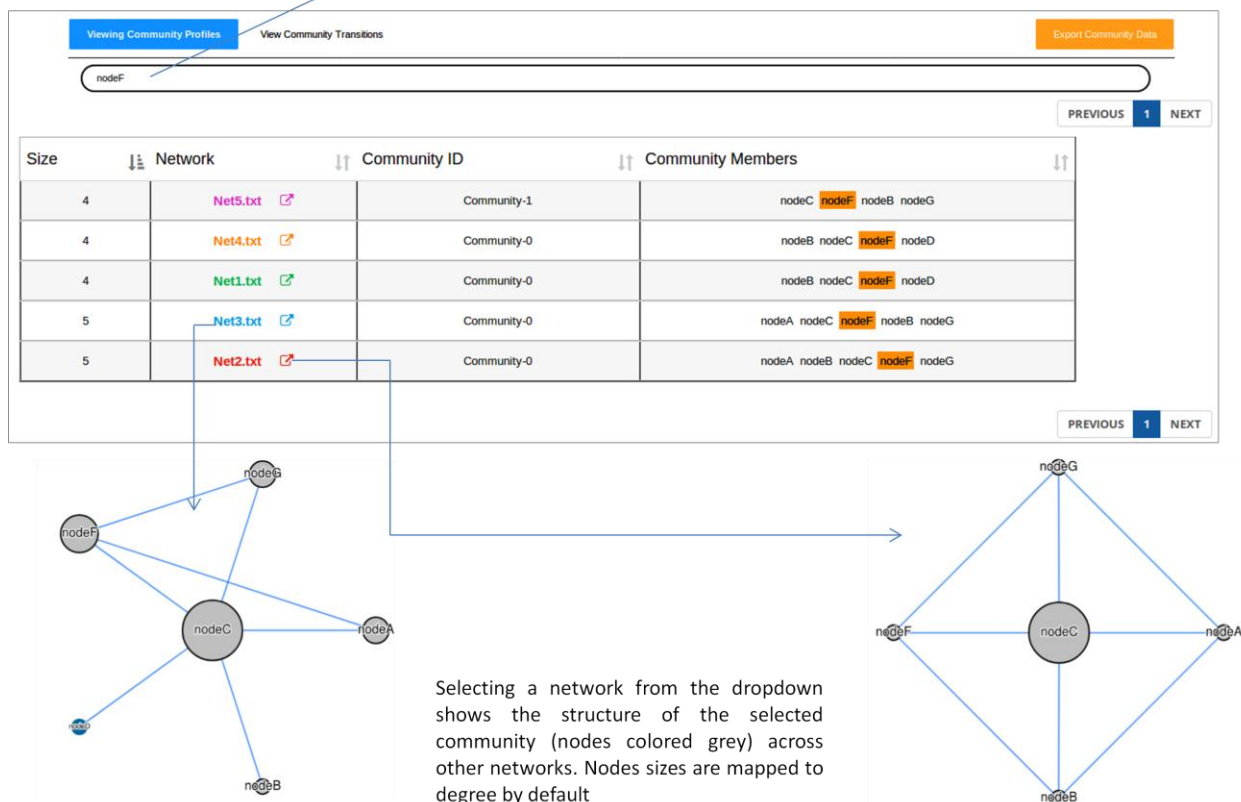
Infer and Compare Community Structures

Objective: This workflow is designed to identify and capture changes in community structure (densely connected group of nodes) across the selection. Communities are inferred using Newman and Louvain algorithms. A 'sankey plot' is used to represent changes in communities between a set of selected networks.

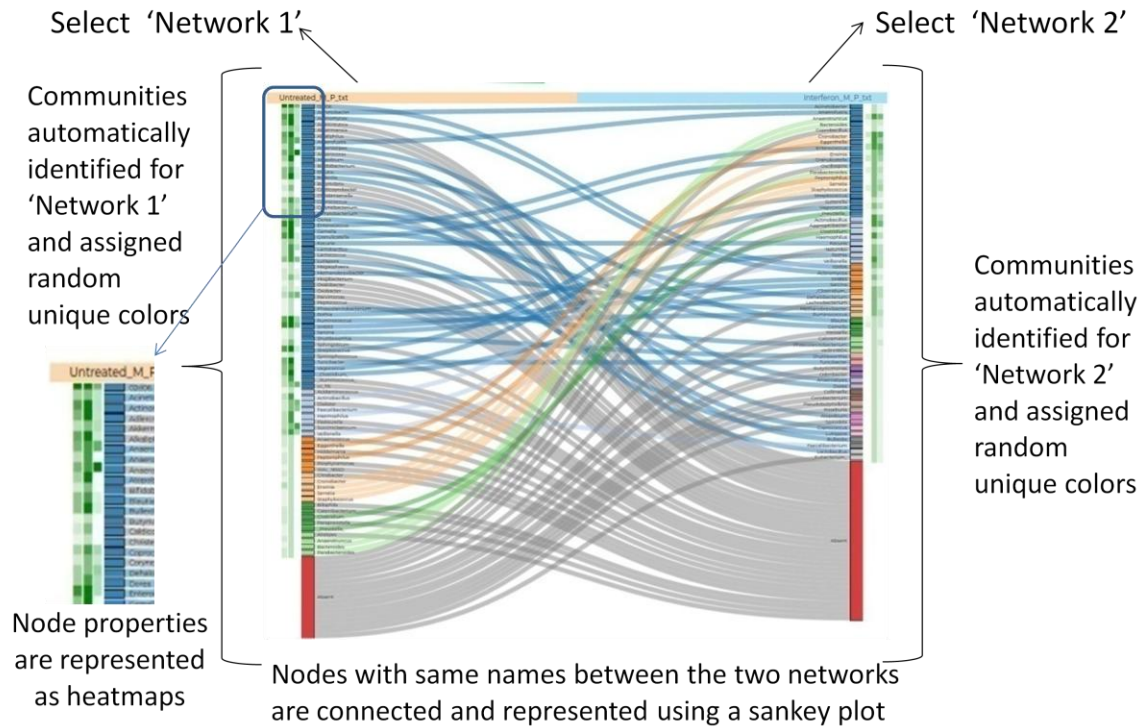
Interpretation:

A comparative analysis of the communities identified in the selected networks can be performed using the features available in this workflow. A list of the identified communities (using both Newman and Louvain algorithms) is presented as a searchable tabulated view. In order to view inter network community shuffling, users need to select two networks from the available dropdown and a community comparison is presented as a sankey plot.

This query searches all communities where nodeF is present. Additional filters like community size & network name can be entered



NetConfer presents the results in the form of ‘Sankey diagrams’ provide an innovative way of visualizing the results for tracking changes in the community composition(s) between a pair of networks



The above Figure represents an example of a heatmap-embedded Sankey diagram based community transition tracking utility of this workflow. In both the vertical axes, the communities (which are easily distinguishable by colors) along with their constituent member nodes are ordered in the descending order of their size. Using the 'node to node' flow between the two vertical axes, changes in communities' constituent can be tracked easily, thereby helping users in identifying not only communities which are conserved across networks, but also the ones which undergo reshuffling. Heatmap embedded besides the nodes represents the three important centrality measures i.e. Degree, Hub-score and Betweenness (whose values have been rank normalized across the given pair of network). This heatmap allows for easy identification of key nodes and tracking their fate in communities of the two networks being compared. Additionally, a tabulated summary of the 'community shuffling' (with an intersection and Jaccard score of community similarity) is presented along with the sum Jaccard and weighted sum Jaccard score for user convenience.

NetConfer Workflow 5

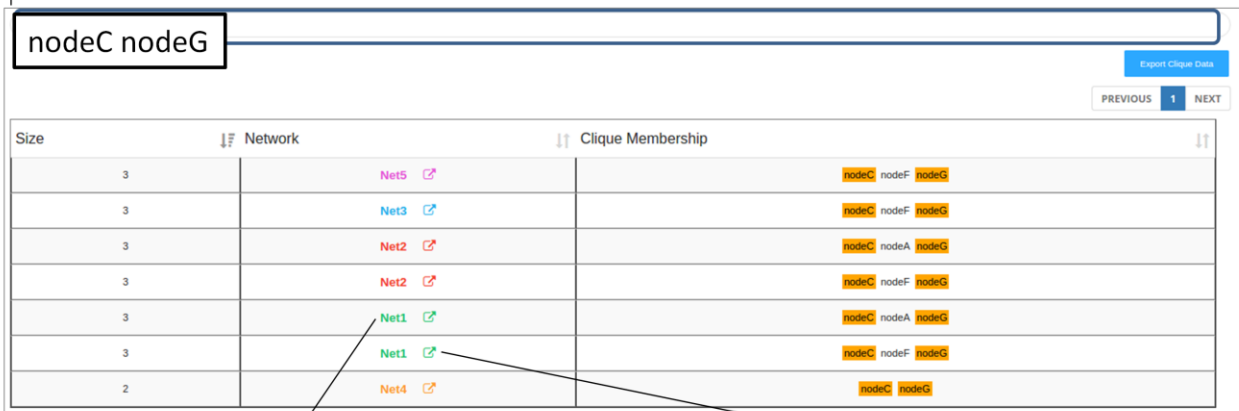
Analysis and Comparison of network Cliques

Objective: This workflow is designed to find and compare 'cliques' (closely knit subset of nodes in a graph) between networks.

Interpretation:

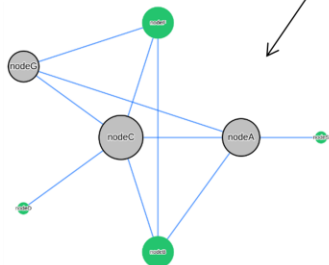
NetConfer automatically finds all cliques in the uploaded networks and presents them as a searchable table. A user can search for cliques having specific members by a powerful yet simplistic query system. Further, the searches can be filtered for a desired set of networks.

Search for one or more nodes to list the cliques where they are present across the selected set of networks. The network names can also be added to narrow down the filter criteria.

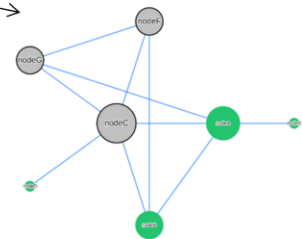


The screenshot shows a search bar containing 'nodeC nodeG'. Below it is a table with columns for Size, Network, and Clique Membership. The table lists several results, with 'Net1' highlighted in green. Arrows point from the search bar and the 'Net1' row to network diagrams below.

Size	Network	Clique Membership
3	Net5	nodeC, nodeF, nodeG
3	Net3	nodeC, nodeF, nodeG
3	Net2	nodeC, nodeA, nodeG
3	Net2	nodeC, nodeF, nodeG
3	Net1	nodeC, nodeA, nodeG
3	Net1	nodeC, nodeF, nodeG
2	Net4	nodeC, nodeG



➤ Clicking on the network names displays the network with the clique highlighted in grey
➤ Similar to communities, the clique structure can be viewed across all the networks



NetConfer Visualization workflows

The intersection and exclusive parts of a selected set of networks can be viewed using the 'Module 1: Intersection Visualization' and 'Module 2: Exclusives Visualization' respectively. The nodes in a network can be easily mapped to various network properties using the 'Module 4: Property Mapped Individual Networks'.

The screenshot displays the NetConfer interface. On the left, the 'Network selector' shows a list of networks (Net1 to Net5) with 'Net4' selected. Below it are 'Network view modifier' icons for zooming and panning. The central area shows a network visualization with nodes labeled nodeA through nodeG. To the right, the 'Network layout and property modifier' panel includes layout options (Hierarchical, Random), node shape options (Circle, Grid, Cose, Concentric), and sliders for 'Change Node Size' and 'Change Font Size'. A text box states: 'Nodes in the network can be easily mapped to various network properties'. At the bottom, a bar indicates 'Nodes are sized by:' with options: Degree (selected), Betweenness, Coreness, Eigenvector, and Eccentricity.

In order to view the union network of a selected set of networks, the 'Module 3: Union Visualization' can be used which displays a network as shown below:

- **Nodes Pie** : Shows the presence of the node across the selected networks
- **Edge gradient** : Shows the presence of the edge across the selected networks

This screenshot shows the 'Union Visualization' of multiple networks. On the left, the 'Network selector' shows five networks (Net1 to Net5) with color-coded boxes. Below it are the same layout and property modifier controls as in the previous screenshot, plus a 'Download' button. The central network visualization shows nodes labeled nodeA through nodeL. Each node is a pie chart where different colored segments represent the presence of that node in the selected networks. Edges between nodes are colored gradients representing the presence of those edges across the selected networks.

A simple yet useful utility to visualize the distance of the individual networks from the global union is implemented in 'Module 5: Distance from the Union'. The distances are calculated as Jaccard indices of the nodes and edges of the respective networks from the global union and presented as a radar chart. The network names are displayed as dimensional anchors placed equidistant on the periphery of a circle. The points on the radial line connecting the center of the circle to each network represent the corresponding distance (node and edge displayed in orange and green color respectively) of that network from the global union

