GNI

Gene Networks International

Cell Illustrator

Gene Net Mode

Reference Manual

Table of contents:

1   Introduction

Since the version 3.0, Cell Illustrator (CI) enables the users to view and analyze gene relationships networks. This functionality is available in the special *Gene Net* mode. The graphical user interface of CI offers the user two modes of working:

(i)   The Biopathway Modeling mode dedicated for simulation and modeling of complex biological processes and systems using Petri Net models. This mode is described separately in the **CI User Guide and CI Reference Manual**.

(ii)   The new Gene Net dedicated for analysis and exploration of gene relationship networks - described in this manual

This manual is a reference for the functional features available in the Gene Net mode. It can be used to answer questions about specific system commands. For installation instructions and an introduction to gene relationship networks, please refer to the User Guide.

The documentation for the Cell Illustrator software includes the manuals listed below:

Cell Illustrator User Guide: Introduction to Cell Illustrator system

Cell Illustrator Reference Manual: Detailed description of Cell Illustrator functions

Cell Illustrator Player Reference Manual: Detailed description of Cell Illustrator Player functions

Cell Illustrator Server Installation Manual: Installation instructions for Cell Illustrator Server product (for IT System Administrators)

Cell Illustrator Gene Net Reference Manual: Detailed description of Cell Illustrator functions (Gene Net mode)

Cell Illustrator Gene Net User Guide: Introduction to the Gene Net mode of Cell Illustrator system

2 Glossary

Gene Network or Gene Relationship Network – a graph that represents the relations between genes. Each graph node represents one gene (or gene transcript), while each edge represents a relationship between the connected genes. For more details see User Guide chapter: Gene Network Elements. Usually, gene networks are inferred by a statistical application which handles a large amount of micro array data.

CI – Cell Illustrator, the software for simulation of Petri Net models of biological processes and pathways.

Gene Net Mode – a mode of CI, which is dedicated to the handling of gene networks. This mode differs from the normal mode dedicated to the building and simulation of biopathway models. Both modes offer a different user interface.

3   Gene Net Mode

This manual describes only the functionality of the *Gene Net* mode. In this chapter it will be described:

- how to switch to the *Gene Net* mode

- what are the differences between the *Gene Net* and *Biopathway Modeling Modes*

- where to find the documentation for the *Biopathway* mode

3.1   Switching to the Gene Net Mode

The menu command View | Gene Net Mode switches between the biopathway modeling and Gene Net modes. If this menu item is checked then you are in the Gene Net mode, otherwise you are in the Biopathway modeling mode.

Any model that has been opened in the CI workspace (or imported) can be viewed in each of both CI modes: Biopathway Modeling and Gene Net mode. However there are the following limitations:

- Do not view large gene networks in the Biopathway Modeling mode

  Displaying large networks with hundreds of edges in the biopathway modeling mode will cause performance problems. Therefore they should be displayed in the Gene Net mode only.

- A typical gene network cannot be simulated.

  Originally a gene network does not contain any data useful for the simulation. After switching to the Biopathway Modeling mode you will see that all simulation parameters for a gene network have default values. Simulating such a net will not give any reasonable results. However such a net can be used as the starting point for creating a simulatable model.

- A biopathway model might not be a correct gene network model

  This is the case if one process has more than one input or output entities, which is normal for Petri net models of biopathways, but forbidden for gene networks. In the case of such a conflict some connection between entities will be ignored. In the Gene Net view one process is represented by one edge connecting the input and output entity of this process. For each process with multiple input or output entities, the edge connects only one input and output entity of the process.

3.2 Differences between Gene Net and Biopathway Modeling Modes

The differences between the Biopathway modeling mode and the Gene Net mode are listed in the table below.

	Biopathway Modeling Mode	Gene Net Mode
Model	Includes 3 base elements: entity, process and connector. Models are created by the user within CI workspace. Biopathway models are smaller but more precisely defined than the Gene Network models. Biopathway models include quantitative simulation properties for studying the kinetics of biological processes.	Includes 2 basic elements: gene and edge. Gene networks are automatically generated by a special external software. Originally gene networks are large models without precise simulation data.
Visualization	More advanced graphics: images for each graph elements, polygon and curved edges for connectors, visualization and animation of simulation progress, etc. Visualization is slower but allows for displaying more details.	Simple graphics: default view styles for each gene and edge. Visualization is faster but includes less details. Thus it is more suitable for large networks.
Editing	Many commands enable building biopathway models from the scratch and defining the simulation properties (e.g. kinetic styles)	Extraction and Merging of subnetworks. Other edit commands are used in seldom cases.
Simulation	Simulation using Petri Net algorithm in interactive or remote mode.	no Simulation capabilities
Analysis	Analysis of simulation	Analysis of gene networks:

	results: charts	Gene Mining, Pathway and Keyword Search, Expression Plot, tools for extraction of subnets

3.3   Documentation for Biopathway Modeling Mode

Please refer to the **Cell Illustrator User Guide** and **Reference Manual** to learn more about the biopathway modeling and simulation capabilities of CI.

4   Workspace in the Gene Net Mode

The Workspace is the main window of Cell Illustrator. It can function in two modes: the original CI mode and the Gene Net mode. The mode of working can be switched by choosing the menu command View | Gene Net Mode. Depending upon which mode is selected the program menus and toolbars are changed. This manual describes the user interface available in the Gene Net mode only.

The Menu Bar located at the top provides a set of commands for building and manipulating a model. Frequently used commands can be also executed by pushing a button on one of the toolbars on the sides of Workspace. Menu items and toolbar buttons corresponding to operations that cannot be performed at that moment are disabled (grayed out).

In the Workspace, multiple model files can be opened simultaneously for viewing and editing. A model file is displayed in a *canvas window*. The canvas window is the main view of the model and allows the model to be edited.

In Cell Illustrator, the user can open several property *dialogs*. The contents of these dialogs reflect:
-   user preferences (applicable to all models),
-   properties of the model in the active canvas window

The list of property dialogs in Gene Net mode is as follows:

Dialog name	Purpose
Element Lists	Displays lists of model elements and values of their main properties.
Element Settings	Allows the viewing and the setting of the properties of a selected element.
External References	Allows for viewing/editing the list of external references
Preferences	Allows the setting of application-wide usage options.
Expression Plot	Displays the expression plot for the selected edge
Partial Residual Plot	Displays the partial residual plot for the selected edge
Graph Layout	Facilitates an automated layout of model elements on the canvas
Subnets	Allows to view, define and combine the subnets in the active canvas.
Keyword Search	Searches for specified elements in the canvas.
Pathway Search	Searches for pathways in the selected network

Gene List Search	Searches for a list of genes in the selected network
Gene Mining	Searches for publications and links for the selected genes

4.1 Menu Bar Commands

4.1.1 File | New

Description:
- Creates a new, empty model.
- The canvas name is "New Canvas *number*", where the number is the number of currently opened models + 1 (this means "New Canvas 1" if there are no canvases at the time the operation is executed)
- CTRL+N is the keystroke shortcut for this command.

4.1.2 File | Open

Description:
- Opens a model from a CSML file.
- CSML file format is the native file format for Cell Illustrator – see www.csml.org.
- It is not possible to open the same file twice. If the user attempts to open a file that is already opened, then the canvas window of that file is activated and displayed in the foreground.
- CTRL+O is the keystroke shortcut for this command.
- The Gene Name property is converted during the file open operation in a special way. The Gene Name is retrieved in the following way:

  - from the Probe Annotation database using the ProbeID.

  - or from the entity name attribute, if the ProbeID could not be found in the Probe Annotation database
- The Probe Annotation database is a file, which contains the mapping of ProbeIDs to Gene Names. In this map each probeID is assigned to one or more Gene Name

4.1.3 File | Open Recent Files

Description:

- Displays a list of recently opened files. Click on an item in the list to open the corresponding file.
- Up to 5 recently opened files are in the list.
- The list does not contain duplicates.
- It is not possible to open the same file twice. If the user attempts to open a file that is already opened, then the canvas window of that file is activated and displayed in the foreground.

4.1.4   File | Close File

Description:
- Closes the active model file without exiting the program.
- If a file has been modified, you are prompted to save the changes before closing the file.
- You are prompted for a file name if you want save a canvas created with the File | New command.
- CTRL+W is the keystroke shortcut for this command.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.5   File | Close All Files

Description:
- Closes all model files without exiting the program.
- If a file has been modified, you are prompted to save the changes before closing the file.
- You are prompted for a file name if you want save a canvas created with the File | New command.
- CTRL+Shift+W is the keystroke shortcut for this command.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.6   File | Save

Description:
- Saves the active canvas in a CSML file under the current filename.
- CSML file format is the native file format for Cell Illustrator – see www.csml.org.

- Use File | Save as, if this command is disabled. E.g. for a newly created or imported canvas

Constraints:
- At least one canvas window must be opened in the workspace.
- You cannot execute this command, if the CSML file does not exist for this canvas. This is the case when the canvas has been created with the File | New or File | Import command.

4.1.7 File | Save as

Description:
- Saves the active file under a new filename selected by the user.
- The file is saved in the CSML file format.
- Use this command to save a newly created or imported file.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.8 File | Import | GN Text File

Description:
- Imports gene networks from a normal text file with tab separated values. The text file should contain the connection table – a list of edges.
- Each row in this text file represents an edge. The edge is described by 4 tab separated values as follows:

  <parent_gene_name> <child_gene_name> <edge_score> <relation_type>

- After importing the text file, the gene network is stored in the CI model and can be saved to a CSML file using the File | Save as command.

4.1.9 File | Export
  ➔ Gene List
  ➔ Path List

Description:
- The commands export, respectively, the list of genes or paths to a file in the CSV format. Such a file can be read by other applications compatible with the CSV format..

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.10 File | Look&Feel
➔ Metal
➔ CDE/Motif
➔ Windows

Description:
- With these commands, you can set the look and feel of Cell Illustrator GUI to a selected style.
- The selected GUI style is preserved upon the restart of the program

4.1.11 File | Print

Description:
- With this command, you can print the whole model diagram and/or expression plots or save them in an image file in PostScript, PNG, or JPEG format.
- The command opens the Print dialog where you select the scope and destination of the print function.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.12 File | Exit

Description:
- Exits the application.
- If any of the opened files have been modified after the last save operation, you will be prompted to save the changes before closing the file.

4.1.13 Edit | Undo

Description:
- Reverses the most recent edit action.
- Execute this command several times to undo the results of subsequent edit commands.
- CTRL+Z is the keystroke shortcut for this command.

Constraints:
- There is an action that can be undone.

4.1.14 Edit | Redo

Description:
- Reverses the action of the last Undo command.
- Effects of subsequent Undo commands are reversed by executing the corresponding sequence of Redo commands
- Shift+CTRL+Z is the keystroke shortcut for this command.

Constraints:
- There is an action to can be redone

4.1.15 Edit | Cut

Description:
- Removes the selection from the active canvas and places it in the clipboard.
- CTRL+X is the keystroke shortcut for this command.

Constraints:
- At least one element must be selected in the active canvas.

4.1.16 Edit | Copy

Description:
- Copies the selected elements into the system clipboard
- The copied elements can be pasted into the same or another canvas in CI workspace
- The gene names of the copied elements can be pasted into any text editor outside the CI workspace
- CTRL+C is the keystroke shortcut for this command.

Constraints:
- At least one element must be selected in the active canvas.

4.1.17 Edit | Paste

Description:
- Inserts the contents of the clipboard into the active canvas
- CTRL+V is the keystroke shortcut for this command.

Constraints:
- At least one canvas window must be opened in the workspace.
- The clipboard must contain elements copied with the Copy or Cut operation.

4.1.18 Edit | Delete

Description:
- Deletes the selected elements from the canvas.
- Del is the keystroke shortcut for this command.

Constraints:
- At least one element must be selected in the active canvas.

4.1.19 Edit | Duplicate

Description:
- Duplicates the currently selected elements in the canvas.
- CTRL+M is the keystroke shortcut for this command.

Constraints:
- At least one element must be selected in the active canvas.

4.1.20 Edit | Extract

Description:
- Copies the selected elements from the active canvas and creates a new canvas with the selected elements.

Constraints:
- At least one element must be selected in the active canvas.

4.1.21 Edit | Select All

Description:
- Selects all objects in the active canvas.
- CTRL+A is the keystroke shortcut for this command.

Constraints:
- The command is disabled if the active canvas is empty.

4.1.22 Edit | Select None

Description:
- Deselects all elements in the active canvas
- Shift+CTRL+A is the keystroke shortcut for this command.

Constraints:
- The command is disabled if the active canvas is empty.

4.1.23 Edit | Select Inverse

Description:
- Inverts the selection in the active canvas.
- CTRL+I is the keystroke shortcut for this command.

Constraints:
- The command is disabled if the active canvas is empty.

4.1.24 Edit | Align Selected Elements to Grid

Description:
- Aligns selected elements to the grid.
- When you insert or move entities they are aligned to the grid automatically. However, changing a grid size (View | Grid Size) may disturb the alignment. Also, the process inserted into the canvas by joining two entities with a connector is sometimes not aligned to a grid. In such a situation, the elements can be aligned using this command.
- See also the related commands: View | Show Grid, View | Grid Size
- CTRL+Shift+G is the keystroke shortcut for this command.

Constraints:
- At least one element must be selected in the active canvas.

4.1.25 Edit | Align all elements to Grid

Description:
- Aligns all elements to the grid
- When you insert or move entities they are aligned to the grid automatically. However, changing a grid size (View | Grid Size) may disturb the alignment. Also, the process inserted into the canvas by joining two entities with a connector is sometimes not aligned to a grid. In such a situation, the elements can be aligned using this command.
- See also the related commands: View | Show Grid, View | Grid Size

Constraints:
- At least one element exists in the active canvas.

4.1.26 Edit | Align to
- → Top
- → Bottom
- → Left
- → Right
- → Vertical
- → Horizontal

Description:
- Aligns all the selected elements in one line to, respectively, the top-, bottom-, left- and rightmost element in the selection.
- *Align the Vertical* and *Horizontal* position of the selected elements along the vertical or horizontal line respectively, in the middle of the selection area.
- *Align to Top* and *Align to Bottom* command the placing of all selected elements in one horizontal line. *Align to Left* and *Align to Right* command the placing of all selected elements in one vertical line.

Constraints:
- At least two elements must be selected.

4.1.27 Edit | Insert Entity
- → Continuous
- → Discrete

➔ Generic

Description:
- Inserts an entity into the active canvas.
- The new entity is positioned in the center of the visible area of the canvas.

Constraints:
- at least one canvas is opened in the workspace

4.1.28 Edit | Insert Image

Description:
- Inserts an image in a JPEG, GIF, or PNG file onto the active canvas. SVG (Scalable Vector Graphics) images can also be inserted.
- In the File Open dialog you can select the file name and type (Image File or SVG Image File) of the image to be inserted. The option "Save Internally" specifies whether the image should be saved internally - inside the model CSML file, or externally – as a reference to an external graphics file.
- The new image is positioned in the center of the visible area of the canvas.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.29 Edit | Insert Text

Description:
- Inserts an empty text box into the active canvas.
- Double-click the text box and enter the text from the keyboard.
- The new text box is positioned in the center of the visible area of the canvas.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.30 Edit | Insert Frame

Description:
- Inserts a rectangular frame into the active canvas
- The new frame is positioned in the center of the visible area of the canvas.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.31 Element | Transform
➔ Rotate
  o 90
  o 180
  o 270

Description:
- Rotates the selected figures (entities, text boxes, frames, etc.) by the specified angle. The rotation center is the center of the rectangular boundary for all the selected items.
- Edges are not rotated. The position of an edge is always adjusted to the position of its start and end elements (genes).

Constraints:
- At least one figure must be selected in the active canvas.

➔ Size

Description:
- Sets the size of the selected figures (genes, text boxes, frames, etc).

Constraints:
- At least one figure must be selected in the active canvas.

➔ Round Corners

Description:
- For frames and hierarchical objects selected in the canvas, the command rounds the corners of their rectangular shapes.

Constraints:
- At least one figure must be selected in the active canvas.

4.1.32 Element | Arrange
➔ Bring to the Front
➔ Bring Forward
➔ Send Backward
➔ Send to the Back

Description:
- With this set of commands, you can set the depth of overlapping figures in the canvas. Depth defines the way in which overlapping figures are displayed. A figure with a lower depth value is displayed over a figure with a higher depth value.
- The depth value of each figure can be viewed and edited in the Element Settings dialog box.
- *Bring Forward* increases the depth value of the selected figures by one.
- *Send Backward* decreases the depth value of the selected figures by one.
- *Bring to the Front* shows the selected figure at the front.
- *Send to the Back* hides the selected figure behind the other figures.

Constraints:
- At least one element must be selected in the active canvas.

4.1.33 Element | Group

Description:
- Assembles two or more selected elements into a single group element.
- A group can be moved or edited as one element.

Constraints:
- At least two elements must be selected in the active canvas.

4.1.34 Element | Ungroup

Description:
- Disassembles a selected group into individual elements.

Constraints:
- At least one group element must be selected in the active canvas

4.1.35 Element | Fill Color

Description:
- Fills the inside of selected figures with the specified color.

Constraints:
- At least one figure must be selected in the active canvas.

4.1.36 Element | Line Color

Description:
- Sets the line color of a selected figure to a color from the list.

Constraints:
- At least one figure must be selected in the active canvas.

4.1.37 Element | Stroke

Description:
- Sets the stroke (line pattern) of selected figures to a pattern from the list of available patterns.

Constraints:
- At least one figure must be selected in the active canvas.

4.1.38 Element | Edit Image

Description:
- Opens the editor for the selected image.
- SVG files are edited by the GLIPS Graffiti SVG editor, which is an integral part of the CI package.
- Other files, JPEG, PNG, and GIFF are edited by the default graphics editor which is associated with the PNG extension of your Windows or Mac OS. On Linux platform the default graphics editor is gimp.
- Standard CI images, e.g. process, entity or connector images cannot be edited. Only images inserted into the canvas from user files can be edited. To insert an image use the commands: Element | Replace Figure | Image or Edit | Insert Image.

Constraints:
- Exactly one editable image must be selected.
- Editable images are images saved in external or internal image files: JPEG, PNG, GIFF or SVG files.

4.1.39 Element | References

Description:
- Displays the list of references available for this element.
- Choose an item from the pop up menu to open the URL in a Web Browser window.
- References define links from the selected element to external resources specified as URLs. Reference may define a link from the selected element to a to database element, such as an entry in a database or a term in a controlled vocabulary
- References can be associated to all elements: genes and edges.
- You can view/edit the list of references by choosing Element | References | Add/Edit URL

Constraints:
- Exactly one element is selected in the active canvas.

4.1.40 Element | References | Add/Edit URL

Description:
- Enables adding new references to the reference list of the selected element.
- This command opens the External References Dialog Box where you can define a reference. You can view the list of references associated with an element in the Element Settings Dialog Box in the *Biological* tab
- URL References can be associated to all elements: genes and edges.

Constraints:
- Exactly one element is selected in the active canvas.

4.1.41 Element | URL Templates

Description:
- Displays the list of URL templates available for this element.
- Choose a link from the list to open the URL in a Web Browser window.
- The URL templates can be associated to genes only. You can view/edit the list of predefined URL templates associated with all genes in the Template | Gene section in the Preferences dialog

Constraints:
- Exactly one gene is selected in the active canvas.

4.1.42 Element | Comments

Description:
- Views the Comments of the selected element.
- This command opens the Comments dialog in which you can view/edit comments for the selected gene/edge.
- You can view the comments associated with an element in the Element Settings.

Constraints:
- Exactly one element is selected in the active canvas.

4.1.43 Element | Text

→ Fill Color
→ Line Color
→ Stroke

Description:
- The Fill Color command sets the text background color for all selected items: elements, text boxes, etc.
- The Line Color command sets the text field border color.
- The Stroke command sets the text field border pattern.

Constraints:
- At least one item must be selected in the active canvas.

4.1.44 Element | Font

→ Name
→ Size
→ Style
→ Color

Description:
- Sets the text font style in all selected items: elements, text boxes, etc.

Constraints:
- At least one item must be selected in the active canvas.

4.1.45 Element | Show Element

➔ On
➔ Off

Description:
- Shows or hides the graphical representation of all selected elements including the child figures, e.g. shows/hides an element and all its labels.

Constraints:
- At least one element must be selected in the active canvas.

4.1.46 Element | Show Name

➔ On
➔ Off

Description:
- Shows or hides, respectively, names of all selected elements.

Constraints:
- At least one element must be selected in the active canvas.

4.1.47 Element | Show Edge Score

➔ On
➔ Off

Description:
- Shows or hides, respectively, the edge score for all selected edges

Constraints:
- At least one edge must be selected in the active canvas.

4.1.48 Element | Show Comment

➔ On
➔ Off

Description:
- Shows or hides the comments of the selected genes.

Constraints:
- At least one element must be selected in the active canvas.

4.1.49 View | Gene Net Mode

Description:
- Switches the Cell Illustrator working mode between the Gene Net and Biopathway Modeling mode
- If this menu item is checked then you are in the Gene Net mode. This manual describes the Gene Net mode
- A network build in the biopathway modeling mode might not be a correct gene network. This is the case if one process has more than one input or output entities, which is normal for Petri net models of biopathways, but forbidden for gene networks. In the case of such a conflict, a warning is displayed when switching from the biopathway modeling to the gene networks view saying the model is not a correct gene network and some connection between entities will be ignored. In the Gene Net view one process is represented by one edge connecting the input and output entity of this process. For each process with multiple input or output entities, the edge connects only one input and output entity of the process.

4.1.50 View | Show Name

Description:
- Shows or hides names of all genes
- This is a global switch. It applies to all canvases inside the CI workspace

4.1.51 View | Show Comment

Description:
- Shows or hides names of all genes
- This is a global switch. It applies to all canvases inside the CI workspace

4.1.52 View | Show Edge Score

Description:
- Shows or hides the edge score for all edges

- This is a global switch. It applies to all canvases inside the CI workspace
- Hiding the edge score speeds up the repaint time for large networks.

Constraints:
- Edge Score is never displayed for large networks with more than 200 edges.

4.1.53 View | Color by Edge Type

Description:
- Switches to a predefined color scheme.
- If this option is selected the edges are colored by the edge type color scheme, which is illustrated on the picture below:
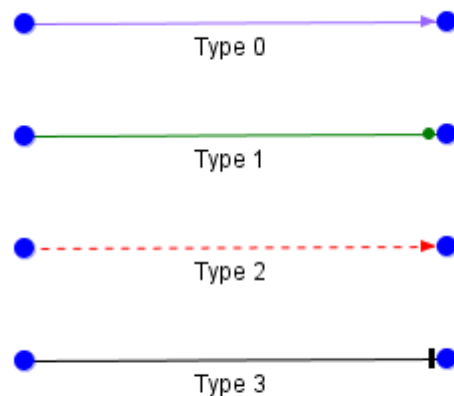
- If this option is not selected edges are displayed in normal colors.
- This is a global switch. It applies to all canvases inside the CI workspace

Constraints:
- This color scheme is not applied if the subnet is not empty. In this case Subnet genes and edges are marked in red. All other genes are displayed in gray. To empty the subnet choose Analyze | Clear Subnet

4.1.54 View | Zoom In

Description:
- The command brings a virtual camera closer to the model in the active canvas
- If necessary, the command will enlarge the canvas by increasing its width and/or height.
- View | Actual Size reverts the canvas to its original scale and size.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.55 View | Zoom Out

Description:
- The command brings a virtual camera farther from the model in the active canvas window.
- View | Actual Size reverts the canvas to its original scale

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.56 View | Fit in Canvas

Description:
- If one or more elements are selected, the command moves the virtual camera to display the selected elements in the canvas window.
- Otherwise, the virtual camera is moved to fit the display of all elements in the active window.
- If necessary, the command will enlarge the canvas by increasing its width and/or height.
- View | Actual Size reverts the canvas to its original scale and size

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.57 View | Actual Size

Description:
- The command moves the virtual camera so that the canvas is displayed with its actual size.
- If necessary, the command will shrink the canvas by decreasing its width and/or height.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.58 View | Show Grid

Description:
-   Toggles the grid display on and off for all canvas windows.
-   The setting is preserved in the user preference settings and also applies when the application is started the next time. See Preferences for more details.

Constraints:
-   At least one canvas window must be opened in the workspace.

4.1.59 View | Antialiasing

Description:
-   Toggles antialiasing on and off for all canvas windows.
-   With the antialiasing in the *on* state, model diagrams look better but it takes more time to draw them.
-   The setting is preserved in the user preference settings and applies also when the application is started the next time. See Preferences for more details.

Constraints:
-   At least one canvas window must be opened in the workspace.

4.1.60 View | Grid Size

Description:
-   Sets the grid size for all canvas windows
-   The setting is preserved in the Canvas section of user preference settings and applies also when the application is started the next time. See Preferences for more details.

Constraints:
-   At least one canvas window must be opened in the workspace.

4.1.61 View | Background Color

Description:
-   Sets the background color for the active canvas windows

Constraints:

- At least one canvas window must be opened in the workspace.

4.1.62 Analyze | Add to Subnet

Description:
- Adds the selected genes and edges to the subnet.
- If an edge is added, both the parent and child gene are additionally added to the subnet
- If a gene is added, all edges that connect this gene with other subnet genes are additionally added
- The color scheme for genes and edges is changed if the subnet is not empty: Subnet genes and edges are marked in red. All other genes are displayed in gray. If the subnet is empty the network genes and edges are displayed in their normal colors.

Constraints:
- At least one element must be selected in the active canvas.

4.1.63 Analyze | Remove from Subnet

Description:
- Removes the selected genes and edges from the subnet
- The color scheme for genes and edges is changed if the subnet is not empty: Subnet genes and edges are marked in red. All other genes are displayed in gray color. If the subnet is empty the network genes and edges are displayed in their normal colors.

Constraints:
- At least one element must be selected in the active canvas.

4.1.64 Analyze | Clear Subnet

Description:
- Removes all genes and edges from the subnet.
- After this operation the subnet is empty.
- The color scheme for genes and edges is changed if the subnet is not empty: Subnet genes and edges are marked in red. All other genes are displayed in gray color. If the subnet is empty the network genes and edges are displayed in their normal colors.

Constraints:

- At least one element must be in the subnet.

4.1.65 Analyze | Extract Subnet

Description:
- Copies the subnet genes and edges from the active canvas and creates a new canvas with the subnet elements only.

Constraints:
- At least one element must be in the subnet.

4.1.66 Analyze | Subnets

Description:
- Opens the Subnets dialog where you can define multiple subnets and manage them, e.g. you may combine subnets by performing logical operation on them

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.67 Analyze | Select | Children

Description:
- Extends the current selection in the canvas by children genes of the selected genes
- Analyze | Add to Subnet creates a subnet consisting o the selected genes and the edges that connect those genes.

Constraints:
- At least one gene must be selected in the active canvas.

4.1.68 Analyze | Select | Parents of Children

Description:
- Extends the current selection in the canvas by selecting genes that have a common children with the currently selected genes
- The children genes are not selected by this command.

- Analyze | Add to Subnet creates a subnet consisting o the selected genes and the edges that connect those genes.

Constraints:
- At least one gene must be selected in the active canvas.

4.1.69 Analyze | Select | Children and Parents of Children

Description:
- Extends the current selection in the canvas by selecting genes that have a common children with the currently selected genes
- The children genes are also selected by this command.
- Analyze | Add to Subnet creates a subnet consisting o the selected genes and the edges that connect those genes.

Constraints:
- At least one gene must be selected in the active canvas.

4.1.70 Analyze | Select | Parents

Description:
- Extends the current selection in the canvas by parent genes of the selected genes
- Analyze | Add to Subnet creates a subnet consisting o the selected genes and the edges that connect those genes.

Constraints:
- At least one gene must be selected in the active canvas.

4.1.71 Analyze | Select | Siblings

Description:
- Extends the current selection in the canvas by siblings of the currently selected genes
- Siblings are genes that have a common parent gene
- The parent genes are not selected by this command.
- Analyze | Add to Subnet creates a subnet consisting o the selected genes and the edges that connect those genes.

Constraints:
- At least one gene must be selected in the active canvas.

4.1.72 Analyze | Select | Parents and Siblings

Description:
- Extends the current selection in the canvas by siblings of the currently selected genes
- Siblings are genes that have a common parent gene
- The parent genes are also selected by this command.
- Analyze | Add to Subnet creates a subnet consisting o the selected genes and the edges that connect those genes.

Constraints:
- At least one gene must be selected in the active canvas.

4.1.73 Analyze | Keyword Search

Description:
- Opens the Keyword Search dialog where you can specify the text to search for gene and edge properties, e.g. you may want to search for genes that have a common gene ontology annotation

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.74 Analyze | Pathway Search

Description:
- Opens the Pathway Search dialog where you can search for subnetworks around the selected gene.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.75 Analyze | Gene List Search

Description:

- Opens the Gene List Search dialog where you can search for a given list of genes.

Constraints:

- At least one canvas window must be opened in the workspace.

4.1.76 Analyze | Merge

Description:

- Merges two or more networks from the canvases in the CI workspace. The merge operation for two networks differs in several details from the merge of multiple networks (more than two). The differences are summarized in the table below:

	Merge 2 Networks	Merge Multiple Networks (more than 2)
Intersection Threshold Parameter	N/A	specified by the use before each merge operation
Merge Result	4 networks: intersection, sum, difference1 and difference2	2 networks: intersection and sum
Colors	After merge edges are colored by 3 color scheme: intersection, difference1 and differeence2	Only the intersection edges are colored after merge

Merge 2 Networks:

- The merge operation compares the two networks and finds the common part of the two networks (intersection) and the differences between the networks and the sum of the two networks (union). The networks are compared by searching for identical genes and edges, the definition of gene and edge identity is described below – see Definitions.
- The merge results are displayed in four new canvases arranged side by side for simultaneous display:

  - the Union of Network 1 and Network 2

  - the Intersection of Network 1 and Network 2

  - the Differences between Network 1 and Network 2

- the Differences between Network 2 and Network 1

- The selected network (Network 1) is treated in a unique way during networks merging: The nodes and edges in the intersection network and also common nodes and edges in the union network inherit their properties from corresponding nodes and edges from the selected network, except for the edge type and color that are defined as stated below.
- The default Color by Relation Type setting is turned off to show edge colors resulting from the network merge operation – see below.
- Edges in Network 1 are marked by one color denoted by the difference in color (default is red) and edges in Network 2 are marked by another color denoted by the difference2 color (default is green). The common edges are marked by the intersection color (default is magenta) in both input networks. The same colors are used for the corresponding edges in the resulting networks. The edges that are common in Network1 and Network2 are colored by the intersection color (default value is magenta). Thanks to this coloring you can easily see, what is the original network of an edge in the merged network.
- The values for the predefined colors difference1, difference2 and intersection can be set in the Preferences dialog box.
- The intersecting edges may be of a different kind in the original networks. In such cases, the resulting type property will be of type 3. Type 3 will denote that the two edges in the original networks conflict.
- The edge colors resulting from the merging operation are persistent, i.e., you can save the output networks and view the edge colors after you open these files.
- The score of common edges can be set to the value of Network1 (default setting) or it can be calculated as the average of merged edges. The way of setting this is defined in the Preferences dialog box. The original score of merged edges is saved in the edge comments as Prior Score.

Merge Multiple Networks (more than 2):
- The merge operation compares all networks and finds the common part of the two networks (intersection) and the sum of the two networks (union). The networks are compared by searching for identical genes and edges, the definition of gene and edge identity is described below – see Definitions.
- After choosing the command, a dialog box is displayed asking you to specify the Intersection Cutoff parameter. This parameter tells, in how many networks a given edge or node must be included to be counted as a common element and displayed in the intersection network.

Merge		×
?	You are about to merge 3 networks. Please specify the threshold for the intersection operation	
	3	
	OK Cancel	
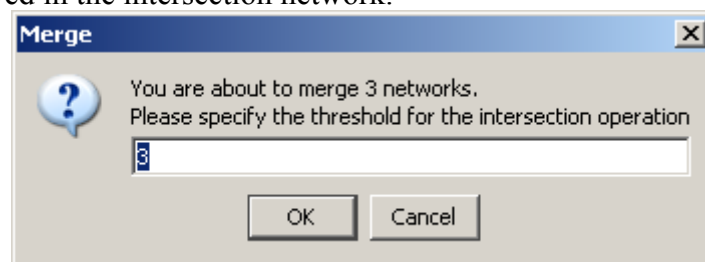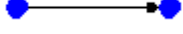
The default value for this parameter is the number of networks to be merged. This is also the maximum value for this parameter. The lower the intersection cutoff, the more edges and genes will be displayed in the intersection network.
- The merge results are displayed in 2 new canvases arranged side by side for simultaneous display:

  - the Union of Network 1, Network 2, Network 3, etc...

  - the Intersection of Network 1, Network 2, Network 3, etc...

Identity Definitions:
- Equality between two nodes: two genes are equal if their corresponding values of *Gene Name* and *ProbeID* are equal
- Equality between two edges: two edges are equal if their corresponding parent and child nodes are equal according to the above definition of the relation of equality between the two nodes.

Edges Types:

Edge Type	Description	View Style
Type 0	up-regulation	
Type 1	down-regulation	
Type 2	Conflict	
Type 3	Unknown	

Constraints:
- At least two networks must be opened in the workspace.

4.1.77 Analyze | Gene Mining

Description:
This command opens the Gene Mining dialog with detailed information about the selected genes in PubMed, KEGG or MIM databases. You can execute this command either for a selected subset of genes or for all genes in the network.

The set of genes upon which gene mining is performed depends on the canvas selection in the following way:

a.   if a gene subnetwork exists on the canvas, then gene mining is performed on the genes of this subnetwork

b.   otherwise, if the normal selection is not empty then gene mining is performed on the set of selected genes

c.   otherwise, if none of the genes in the network are selected, the gene mining is performed on all genes in the network.

After executing this command, you should see Processing Database dialog after which the Gene Mining dialog is displayed with the search results.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.78 Analyze | Expression Plot

Description:
- Opens the Expression Plot window for the selected edge..

Constraints:
- Exactly one edge or two nodes must be selected in the active canvas.

4.1.79 Analyze | Partial Residual Plot

Description:
- Opens the Partial Residual Plot window for the selected edge..

Constraints:
- Exactly one edge must be selected in the active canvas.

4.1.80 Dialog | Hide All Dialogs

Description:
- Closes all property dialogs

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.81 Dialog | Element Lists

Description:

- Toggles on and off the display of the Element Lists dialog
- The contents of the dialog correspond to the active canvas window.
- The dialog receives the focus if it is opened.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.82 Dialog | Element Settings

Description:
- Toggles on and off the display of the Element Settings dialog
- The contents of the dialog correspond to the current selection in the active canvas window
- The dialog receives the focus if it is opened.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.83 Dialog | Preferences

Description:
- Toggles on and off the display of the Preferences dialog
- The dialog receives the focus if it is opened.

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.84 Dialog | Graph Layout

Description:
- Toggles on and off the display of the Graph Layout dialog
- The opened dialog receives the focus

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.85 Window | Cascade Canvases

Description:
  - The command cascades canvas windows.

Constraints:
  - At least one canvas window must be opened in the workspace.

4.1.86 Window | Tile Canvases

Description:
  - The command tiles canvas windows.

Constraints:
  - At least one canvas window must be opened in the workspace.

4.1.87 Window | Minimize All Canvases

Description:
  - The command minimizes all canvas windows

Constraints:
  - At least one canvas window must be opened in the workspace.

4.1.88 Window | Maximize All Canvases

Description:
  - The command maximizes all canvas windows.

Constraints:
  - At least one canvas window must be opened in the workspace.

4.1.89 Window | Duplicate Canvases

Description:

- The command duplicates an active canvas window by creating a new view for the same model file
- The name of the new window is the name of the original window with "+"
- All duplicate canvases represent the same model. Thus, any modification of the model in one canvas is immediately updated in all the duplicate canvases.
- File | Close File closes all the duplicate canvases that correspond to the active canvas

Constraints:
- At least one canvas window must be opened in the workspace.

4.1.90 Help | Cell Illustrator Help

Description:
- Opens the HTML help system for Cell Illustrator.

4.1.91 Help | Cell Illustrator User Guide

Description:
- Opens the Cell Illustrator User Guide.

Constraints:
- The User Guide is a PDF document. Adobe Acrobat Reader or alternative software capable of reading PDF documents needs to be installed and configured on your machine.

4.1.92 Help | Cell Illustrator Online

Description:
- Opens the home page for the Genomic Object Net (GON) project in the default browser.
- GON is the research project at the University of Tokyo that drives the development of Cell Illustrator.

Constraints:
- The Internet connection must be available.

4.1.93 Help | GNI Website

Description:
- Opens the home page of GNI Ltd.

Constraints:
- An Internet connection must be available.

4.1.94 Help | About Cell Illustrator

Description:
- Displays the dialog About Cell Illustrator with the version and license information

4.2   CI Toolbars

4.2.1   Edit Toolbar

This toolbar is located at the top of the main window and contains a set of buttons for the most frequent edit operations.

Icon	Button Name	Description
	Selection Mode	In this mode, you can select elements on the canvas with the arrow cursor.
	Create Gene	Push this button and click on the active canvas to insert a gene. Each subsequent click adds a new gene.
	Create Edge	Push this button and draw a line between two genes on the active canvas to insert an edge.
	Create Frame	Push this button and drag the mouse cursor onto the active canvas to insert a frame
	Create Note	Push this button and drag the mouse cursor on the active canvas to insert a text note.
	Manual Move	Switches Cell Illustrator to the mode, where you can change the visible area of the active canvas by dragging the canvas with the mouse.
	Zoom In	In this mode, click on the active canvas to zoom in.
	Zoom Out	In this mode, click on the active canvas to zoom out.
	Reset Zoom	See View	Actual Size
	Fit To Canvas	See View	Fit in Canvas
	Group	See Element	Group
	Ungroup	See Element	Ungroup
	Insert Image	See Edit	Insert Image
	Set Color	Click on the popup list of colors to apply the color to selected elements on the

Icon	Name	Description
	Select Color Tool	With this button, you can select the Fill Color, Line Color or the Text Color as the current setting for the Set Color command
	Set Stroke	The command applies a stroke from a drop-down list to selected elements on the canvas.
	Toggle the Antialiasing Status	See View | Antialiasing
	Toggle the Grid's Visible Status	See View | Show Grid

4.2.2 File Toolbar

This toolbar is located on the left side of the main window, above the Undo/Redo toolbar. It consists of a set of buttons for file management operations.

Icon	Toggle Button	Name	Full Description
	No	Create New Canvas	See File | New
	No	Open Canvas File	See File | Open
	No	Close Canvas	See File | Close File
	No	Save Active Canvas	See File | Save
	No	Save Canvas To Selected File	See File | Save as
	No	Close All Canvases	See File | Close All Files

4.2.3 Undo/ Re-Execute Toolbar

This toolbar is located on the left side of the main window, below the File Toolbar. It contains buttons for Undo/Redo and Align commands.

Icon	Name	Description
	Undo	See Edit | Undo
	Redo	See Edit | Redo
	Align Top	See Edit | Align to
	Align Bottom	See Edit | Align to
	Align Left	See Edit | Align to
	Align Right	See Edit | Align to
	Align Vertical	See Edit | Align to
	Align Horizontal	See Edit | Align to

4.2.4   Dialog Toolbar

This toolbar is located on the right side of the main window and contains buttons that open and close property dialog windows.

Icon	Name	Description
	Toggle Element Lists Visible Status.	See Dialog | Element Lists
	Toggle Element Settings Visible Status	See Dialog | Element Settings
	Toggle References Visible Status	See Element | References
	Toggle Preferences Visible Status	See Dialog | Preferences
	Toggle Graph Layout Visible Status	See Dialog | Graph Layout
	Toggle Subnets Visible Status	See Analyze | Subnets
	Toggle Keyword Search Visible Status	See Analyze | Keyword Search
	Toggle Pathway Search Visible Status	See Analyze | Pathway Search
	Toggle Gene List Search Visible Status	See Analyze | Gene List Search
	Toggle Expression Plot Visible Status	See Analyze | Expression Plot
	Toggle Partial Residual Plot Visible Status	See Analyze | Partial Residual Plot

	Toggle Gene Mining Visible Status	See Analyze | Gene Mining
	Hide all dialog windows	See Dialog | Hide All Dialogs

5 Drawing Canvas

The canvas window is the location where you can view/edit a model. In addition to commands available in the Menu Bar and the toolbars, you can right click (CTRL click on a Macintosh) on the canvas or on a selected element in the canvas to access a popup menu customized to your selection.
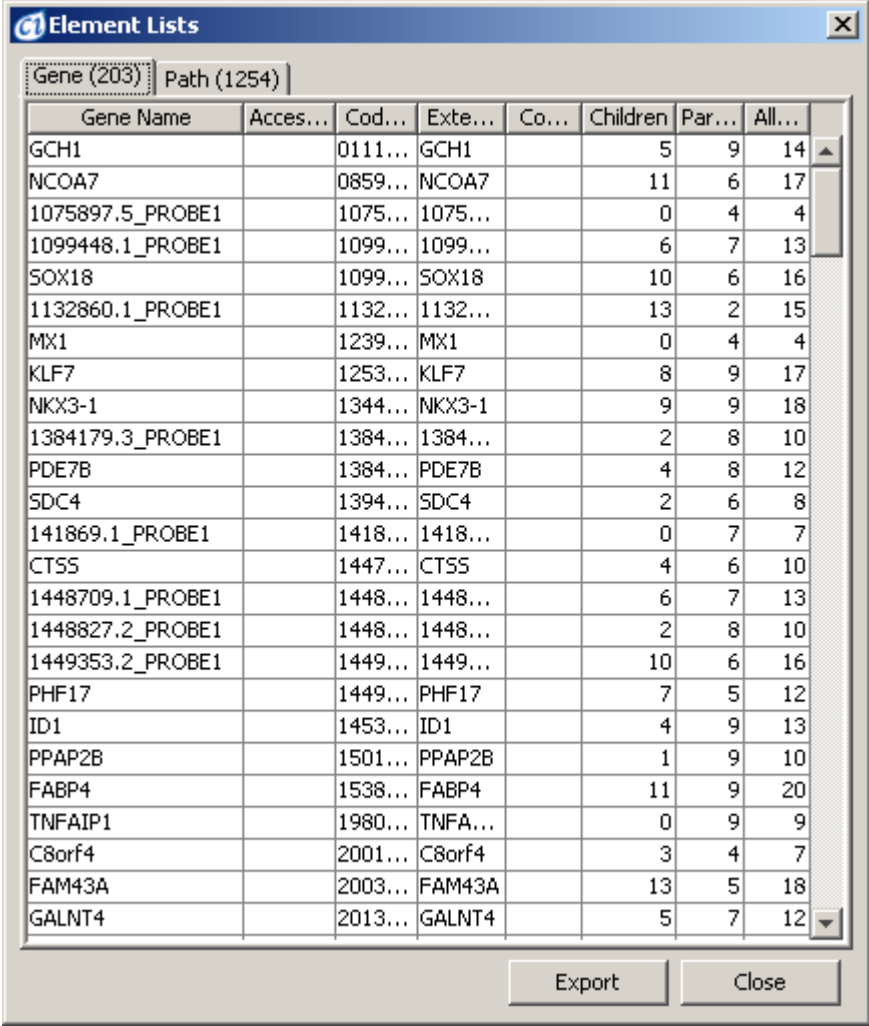
You can customize the background color and other properties of your canvas windows by editing the Canvas section of the application global settings in the Preferences dialog.

5.1 Canvas Popup Menus

Selection	Popup Menu
Canvas	Select All

	Paste

	Background Color

	Duplicate Canvas
Gene	Add to Subnet
	Remove from Subnet

	Cut
	Copy
	Delete
	Duplicate

	Arrange

	Element Settings

	References
	Comments
	Element | URL Templates

Edge	Add to Subnet
	Remove from Subnet

	Cut
	Copy
	Delete
	Duplicate

	Arrange

	Element Settings

	References
	Comments
	Expression Plot
	-------------

6 Element Lists

For the model in the active canvas, the Element Lists modeless dialog displays lists of genes and edges together with values of their major properties. Switching between canvas windows results in an update of the tables.

The *Element Lists* dialog box in the Gene Net mode consists of the tabbed tables *Gene, Path* and the *Export and Close* controls.

Each column in a table can be sorted by clicking its column header.

6.1.1 Gene Table

Each row in the table corresponds to a gene in the active canvas. The following properties are listed in the table:
- o Name – gene name
- o Accession – the accession value
- o ProbeID – the unique probe ID associated with the gene
- o Extension – additional description of the gene
- o Comments – additional description of the gene

- o   Children – the number of child genes connected with this gene
- o   Parents – the number of parent genes connected with this gene
- o   Edges – the number of all the edges connected with this gene

6.1.2   Path Table

Each row in the table corresponds to an edge in the active canvas. The following edge properties are listed in the table:
- o   Parent – the number of the parent (source) gene of this edge
- o   Child – the number of the child (target) gene of this edge
- o   Edge Score – the edge score value
- o   Comments – additional description of the gene

6.1.3   Export Button

This command exports the selected table of genes or edges to a CSV file.

6.1.4   Context Menu

The context menu opens on the right click of the table. It includes the following commands that apply to the currently selected genes/edges:

- Add To Subnet – adds the selected genes/edges to the subnet

- Remove from Subnet – removes the selected genes/edges from the subnet

- Delete – deletes the selected genes/edges

- Copy Selection to Clipboard – copies the selected row to the clipboard as tab separated values

7 Element Settings
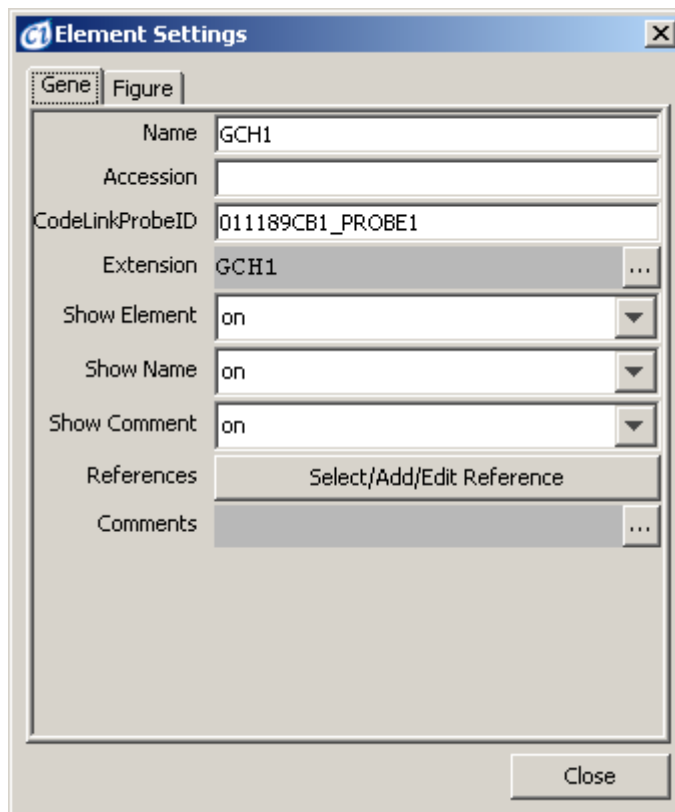
The Element Settings is a modeless dialog that allows the viewing and setting of the properties of a selected element:
- If a single gene or edge is selected, the dialog displays its properties. Otherwise the dialog shows the global properties of the model in the active canvas.
- Change of selection or switching between canvas windows results in an update of the dialog.
- Changing a setting in the dialog has an immediate effect in the model.
- The display properties associated with an element are preserved in the model file and override the global view settings.

7.1 Model and Canvas Property Sheet.

This tab displays a number of properties describing the model in the active canvas and the canvas window itself. These properties cannot be edited.

7.2 Gene Property Sheets

For a selected gene, its properties are presented in the Gene Sheet and the Figure Sheet.

7.2.1 Entity Sheet

Property Name	Description
Name	Gene Name
Accession	Accession Number
ProbeID	The unique probe ID associated with the gene.
Extension	Additional description of the gene
Show Element	Turns the display of the whole element on and off. This setting is preserved in the model file and overrides the global view settings.
Show Name	Turns on and off the display of the whole element.
Show Comments	Turns on and off the display of the comments associated with the gene
References	List of URL sites related to the entity
Comments	Comment field

7.2.2 Figure Sheet

Property Name	Description
Name	Gene name
Size	Size of the figure in pixels. The figure width and height are *given* as two integer values separated by the space character.
Fill Color	Color of the figure
Line Color	Color of the border line
Stroke	Type of the border line

7.3 Edge Property Sheets

For a selected edge, its properties are presented in the Edge Sheet and the Line Sheet.

7.3.1 Edge Sheet
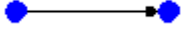
Property Name	Description
Name	Internal name of the edge
Type	The type of the relation. It can be: - Type 0 – the expression of the target gene is stimulated by the source gene - Type 1 – the reverse of Type 0, where the expression of the target gene is blocked by the

	source gene
	- Type 2: unknown - neither Type 0 nor Type 1.
	- Type 3: conflict during merge – two merged
	The default value is Type 0.
Edge Score	The edge score.
Show Element	Turns on and off display of the whole element
Show Score	Turns on and off display of the edge score.
References	List of URL sites related to the entity.
Comments	Comment field

7.3.2   Line Sheet

Property Name	Description
Name	Internal name of the edge
Line Color	Color of the border line
Stroke	Type of the border line

7.3.3   Edge Type View Style

Edge Type	Description	View Style
Type 0	up-regulation	
Type 1	down-regulation	
Type 2	Conflict	
Type 3	Unknown	

8 Preferences
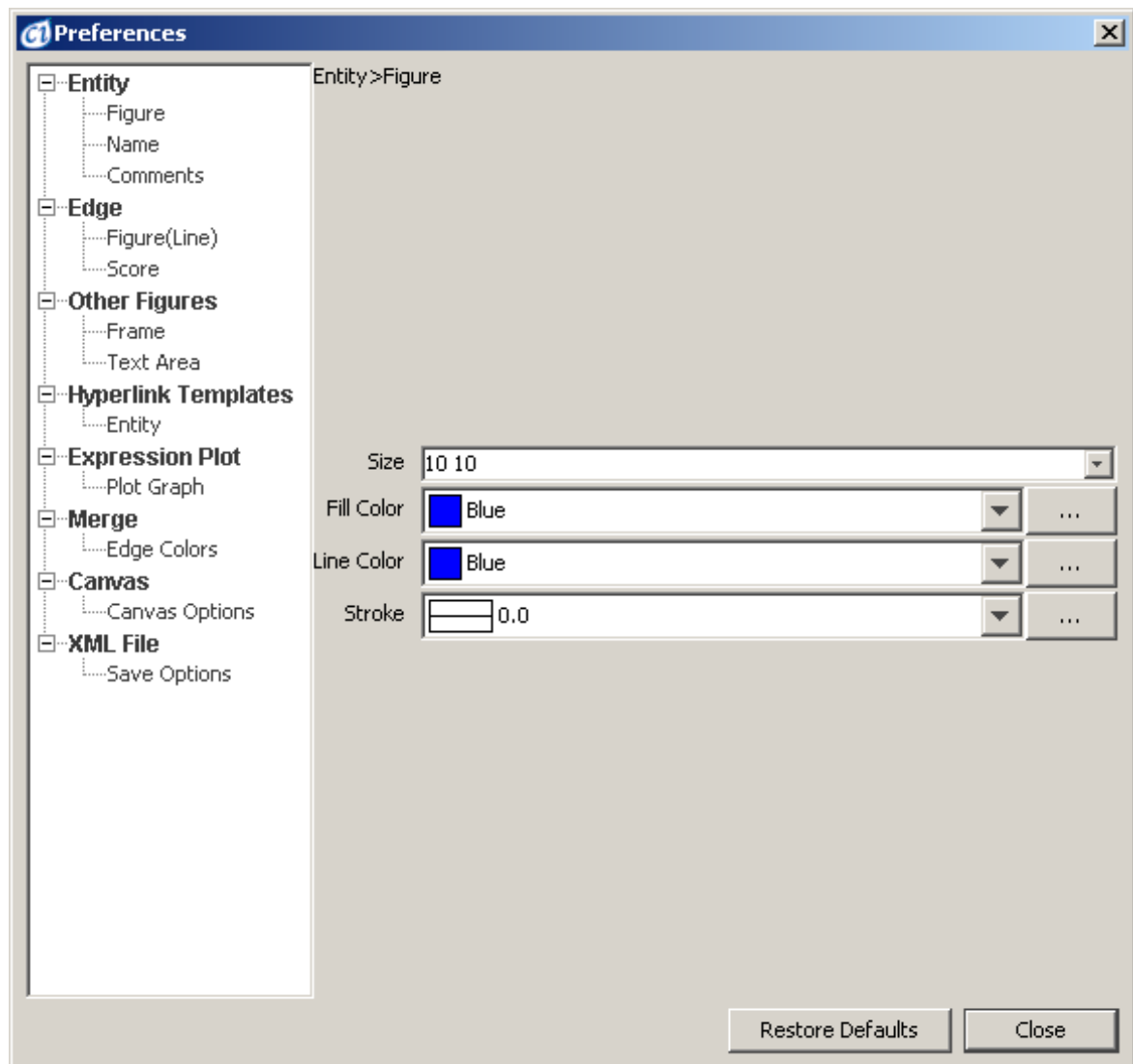
With the Preferences dialog, you can set the global properties of the Gene Net mode. The settings are stored as user preferences and also apply the subsequent occasion you start the application. A change in the Preferences dialog is effective immediately and applies to new elements, canvas windows and simulations runs that are executed after the change unless the setting is one designated for the whole application, such as grid size. With such cases, the setting applies to all (already existing and new) canvas windows. The *Restore Defaults* button restores the default (factory) settings for the selected branch of the option tree.

9 Graph Layout

Using this dialog, you can "beautify" the graph layout of the model in the active canvas.

To change the layout of a model you need to take the following steps:

- Open the Graph Layout dialog

- Import the model into the Graph Layout dialog box

- Run one of the available layout algorithms

- Export the new layout.
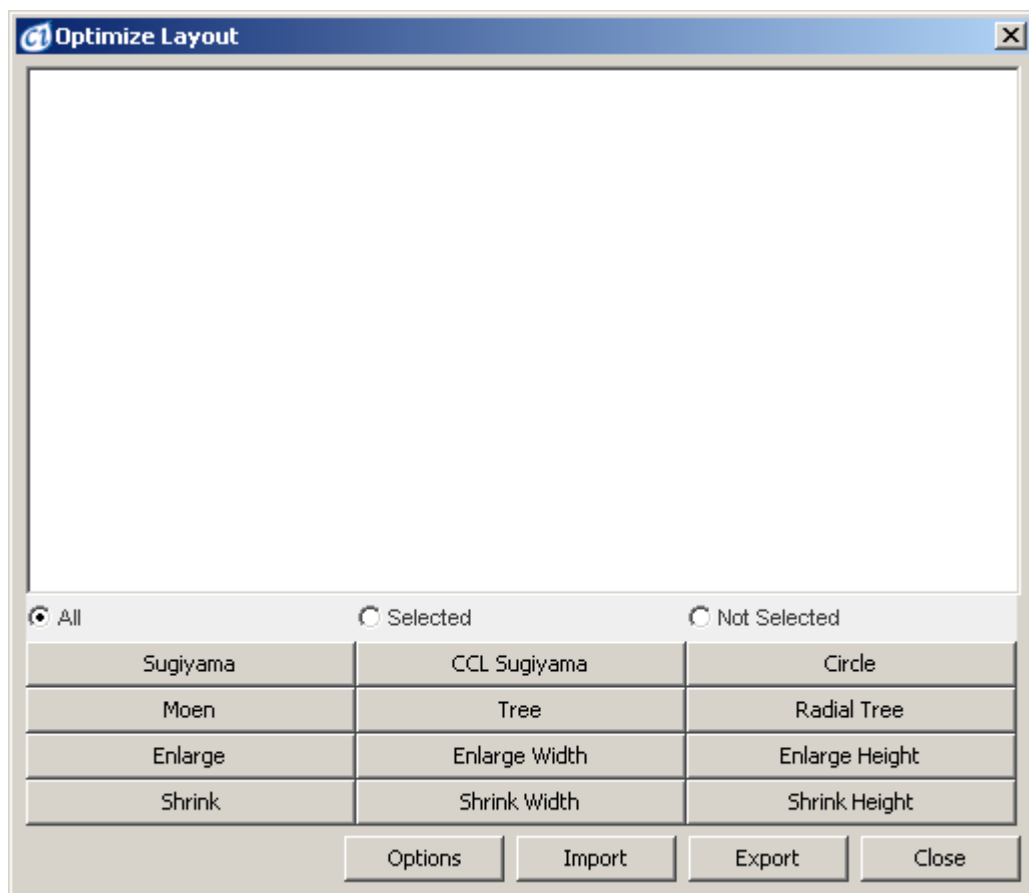
The buttons at the bottom of the dialog are used to perform the following commands:

- *Import* – imports the whole model from the active canvas to the Graph Layout dialog box.

- *Export* – exports the graph from the Graph Layout dialog box to the canvas. This operation updates the positions of the elements in the canvas to the positions that have been set in the Graph layout dialog box.

- Each of the buttons *Sugiyama, CCL Sugiyama, Circle, Moen, Tree, Radial Tree* executes the layout algorithm for the graph that is displayed in the Graph Layout dialog. Depending on the selected radio button, the layout algorithm can "optimize" the positions of *all* nodes, the *selected* nodes only or the *others, i.e.,* unselected nodes. The node selection should be executed inside the small canvas with standard mouse operation.

9.1 Graph Layout Algorithms

A brief description of each graph layout algorithm is given in the table below.

Layout Name	Description
Sugiyama	Nodes are organized in levels according to their parent child relation as in a company organization chart. Nodes without parents are at the top. A child node is always below all of its parent nodes.
CCL Sugiyama	CCL stands for Child Count Layout. Nodes are organized in levels according to their child count. Nodes with the most children are at the top. Nodes with the same number of children are in one row. In this layout a child node can be above its parent.
Circle	Nodes are positioned on a circle
Tree	Requires the selection of one node inside the Graph Layout window. This node becomes the root (starting point) of the tree. The tree is constructed by placing connected nodes below the current node. The edge direction (parent-child or child parent) does not matter.
Moen	Improved tree layout
Radial Tree	A tree layout converted to a circle. The tree root is in the middle of the circle.

Both tree layouts, called Tree and Moen, require the selection of one node inside the Graph Layout window as the starting point for the tree.

10 Keyword Search

Using this dialog, you can locate genes and edges containing the specified text in one of their properties. The keyword search is performed by execution of the following steps:

- Enter a search string into the Search For edit box,

- Select search options using the checkboxes

- Select the properties to be searched for, in the Search In panel.

- Press the Find button.

- Right click on the Search Result list to perform the operation on the discovered elements.
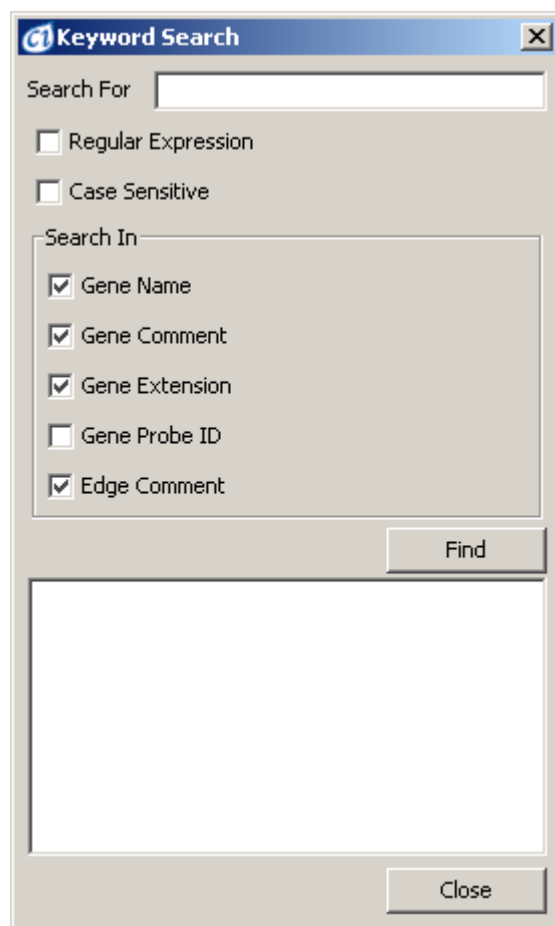
The Finder is a modeless dialog. After finding an element, the user can switch back to the canvas window and edit the element without closing the Finder window.

- Regular expressions can be used to find groups of similar elements.

- Elements found in the search process are displayed in the Search Results list box at the bottom of the dialog. Also, the number of found objects is displayed above the list box.

- Clicking an item in the Search Results list box selects the corresponding element in the workspace. CTRL+click (Apple+click on Mac) and SHIFT+click allow for selecting/deselecting multiple items.

- To select an object, the canvas that has been searched must be active. If the active canvas is changed after the search, the Search Results list is cleared.

- The Close button dismisses the dialog window.

10.1.1 Context Menu

The context menu opens on the right click of the table. It includes the following commands that apply to the currently selected genes/edges:
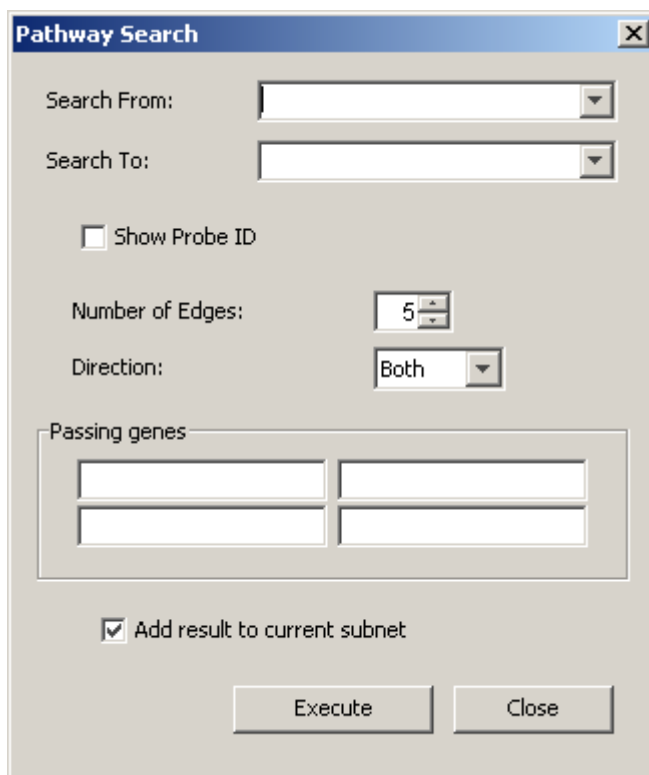
- Add To Subnet – adds the selected genes/edges to the subnet

- Remove from Subnet – removes the selected genes/edges from the subnet

- Delete – deletes the selected genes/edges

11 Pathway Search

Using this dialog, you can find subnetworks around the specified gene or gene-to-gene pathways. The pathway search is performed by the execution of the following steps:

- Select a gene in the Search For combo box.

- Select a target gene in the Search To combo box. This step is optional. Leave the Search To field empty, if you want to find a subnetwork around the specified gene.

- Specify the Number of Edges to be searched for.

- Specify the search Direction.

- Specify the auxiliary options Passing Gene

- Select whether to add results to the current subnet.

- Press the Execute button.

11.1 Search From Combo Box

In this combo box you can select the starting gene for each search. This combo box contains list with all genes in the active canvas.

11.2 Search to Combo Box

In this combo box you can select the target gene for each search. This combo box contains the list with all the genes in the active canvas.

If this field is empty, the target gene can be any gene in the canvas and the search results will include all pathways beginning in the Search From.

If this field is not empty the search results will include only those pathways that start in the Search From gene and end in the Search To gene.

Use this field, if you want to find a pathway between two genes (gene-to-gene pathways) only. Otherwise, if you want to find a subnetwork around the starting gene leave this field empty.

11.3 Show Probe ID

This options changes the information displayed in the gene lists in the Search From and Search To combo boxes. If the option Show Probe ID is selected, then each gene is represented as a pair Gene Name and Gene Probe ID in the gene list. Otherwise only the Gene Name is displayed in the gene list.

This option is useful when handling ambiguous situations. In rare cases, two genes may have the same Gene Name, but they will possess different Probe IDs.

11.4 Number of Edges

In this field you specify the number of edges to be searched for. To search for the nearest neighbors only, specify 1. To search for the nearest neighbors plus their nearest neighbors specify 2. The larger the number of edges the more search results you will receive.

11.5 Direction Combo Box

In this combo box you specify the search direction. You may choose one of the following 3 possibilities:

- Forward - to search for child genes only.

- Reverse - to search for parent genes only

- Both to search for any related genes.

11.6 Passing Genes

A Passing Gene is a gene that must be included in the Search Results pathways. You may define up to 4 Passing Genes.

11.7 Add Results to Current Subnet

Select this option to maintain the current subnet. If this option is checked the current subnet will be preserved after finishing the pathway search.

11.8 Execute Button

This starts the search with the specified options. The discovered pathways are displayed in the Pathway Search Results dialog box.

12 Pathway Search Results

This dialog box displays the list of pathways that have been discovered during the Pathway Search.

Each pathway is displayed in one row and described by the following properties:

- column 1: pathway length – the number of edges in the pathway

- column 2: the first gene in the pathway – the gene specified in the Search From field

- column 3: edge direction – the direction of the edge between the first gene (column 2) and the second gene (column 4)

- column 4: the second gene in the pathway

- column 5: edge direction – the direction of the edge between the second gene (column 4) and the third gene (column 6)

- column 6: the third gene in the pathway

- etc.

Click a row in the table to add the corresponding pathway to the subnet. CTRL+click (Apple+click on Mac) and SHIFT+click allow for the addition or removal of multiple items to the subnet.

13 Subnets

In this dialog, you can view the list subnets of the active canvas (model) in the CI workspace. Each subnet is described by its name. The name is a unique identifier and can be defined by the user.
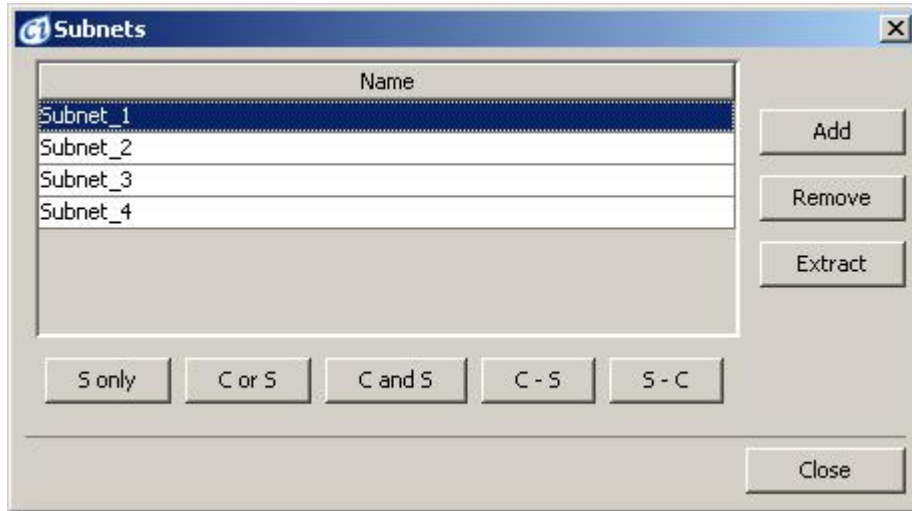
In this dialog you may also define a new subnet. To define a new subnet, select the desired nodes and edges on the canvas and then press the *Add* button. This will add a new item to the Subnet list with an auto-generated name. The generated name can be changed by double clicking on the item. The defined subnets are stored in the CSML file after saving the model.

The other buttons allow you to manage the list of registered engines:

- *Remove* – removes the selected subnet from the list

- *Extract* – extracts the selected subnet to a new canvas

- *Edit* – facilitates the changing of the server properties, e.g. the URL, user name or password.

The *Logical Operation* buttons allow to combine the subnet currently selected in the canvas (C) with the subnet selected in the subnet list. The results of these operations are displayed on the canvas as a new subnet.

***S only* button**

Selects the subnet selected in the list on the canvas.

***C or S* button**

Adds the subnet selected in the subnet list (S) to the subnet selected in the canvas (C)

C and S button

Creates a new subnet on the canvas that is the intersection of the subnet selected in the canvas (C) and the subnet selected in the subnet list (S)
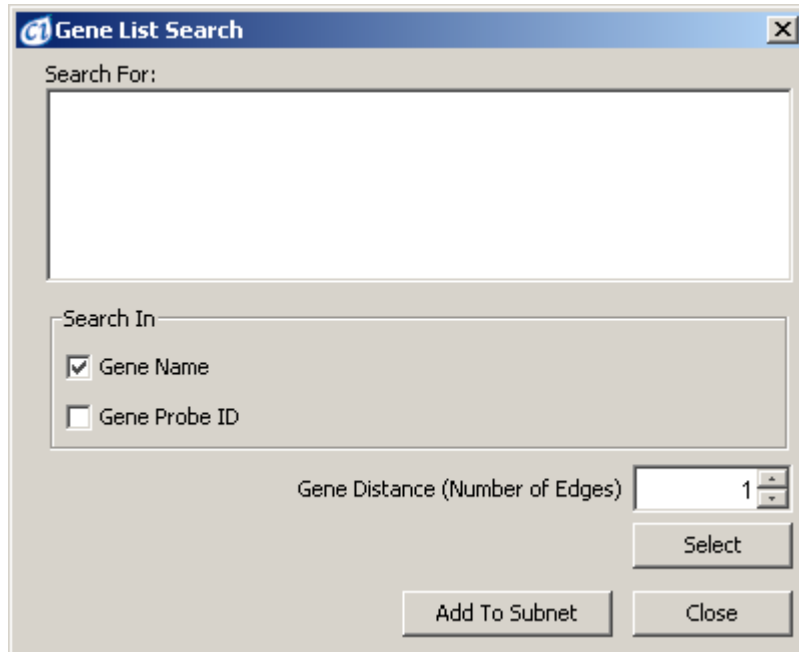
C – S button

Creates a new subnet on the canvas that is the logical difference of the subnet selected in the canvas (C) and the subnet selected in the subnet list (S)

S – C button

Creates a new subnet on the canvas that is the logical difference of the subnet selected in the subnet list (S) and the subnet selected in the canvas (C)

.

14 Gene List Search

Using this dialog, you can locate a subnet by specifying a list of gene names or probe IDs.

The search is done in the following steps:

- Open the Gene List Search dialog box. This can be done by clicking the *GL Search* button on the right toolbar or by choosing Analyze | Gene List Search

Note: The *Search For* edit box is initialized by the names of the currently selected genes. This is useful if you want to search for a subnet that consists of the selected genes and their connections within a given distance of edges.

- Enter (paste) the list of names into the *Search For* edit box

Note: After copying nodes of one canvas (see Edit | Copy), you may paste the list of their names into any text editor, including the *Search For* edit box.

- Select where to search by choosing the options in the *Search In* box

- Specify the *Gene Distance* in edges. For the default value 1 only edges that directly connect the found genes will be selected. If the specified edge distance is larger than one then all paths (gene-edge-gene-edge-gene-...) connecting found genes within the given number of edges will be selected. The larger the *Gene Distance* value the larger the found subnetwork (more genes and edges will be selected)

- Press the *Select* button. The gene/probe names might be separated by any standard separator, such as space, tab, coma, semicolon, new line. The gene

name list to be searched for is usually copied from an external database or spreadsheet or from another canvas.

- The found subnetwork is highlighted on the canvas with the selection color (green is the default). After inspecting the search results on the canvas, you may change the search criteria (e.g. the *Gene Distance*) and resume the search by clicking the *Select* button.

The *Add To Subnet* button adds the found genes to the subnet selection. Also the edges that connect the found genes are added to the subnet selection.

The *Close* button dismisses the dialog window.

15 Expression Plot
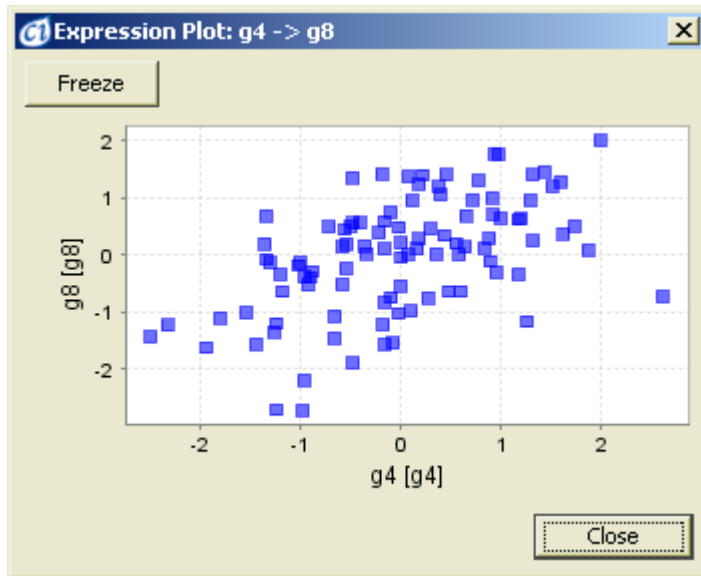
     This dialog visualizes the expression plot for the selected edge or for the selected gene pair. The expression plot displays more detailed information about the results of the micro array experiments, which have been executed to obtain this gene network.

Note: The expression plot is specific for the GNI technology of generating gene networks. The plot requires additional micro-array experiment data. Without this data the expression plot cannot e viewed.

     The expression plot requires the expression plot file with additional experimental data that is not included in the gene network file.

     To view the expression plot:

1. Make sure that the expression plot file is available in CI.

    For this, open the Preferences dialog box and check that the Expression Plot File location is correctly defined in the Expression Plot section.

2. Select an edge on the canvas. Alternatively you may select any two genes.

Note: The expression plot can be viewed for any two genes, regardless if they are connected by an edge or disconnected.

3. Choose Analyze | Expression Plot from the menu or the Expression Plot icon from the right side toolbar

4. Press the Freeze button to keep the selected expression plot

5. Select another edge (or two genes) to view its expression plot.

16 Partial Residual Plot
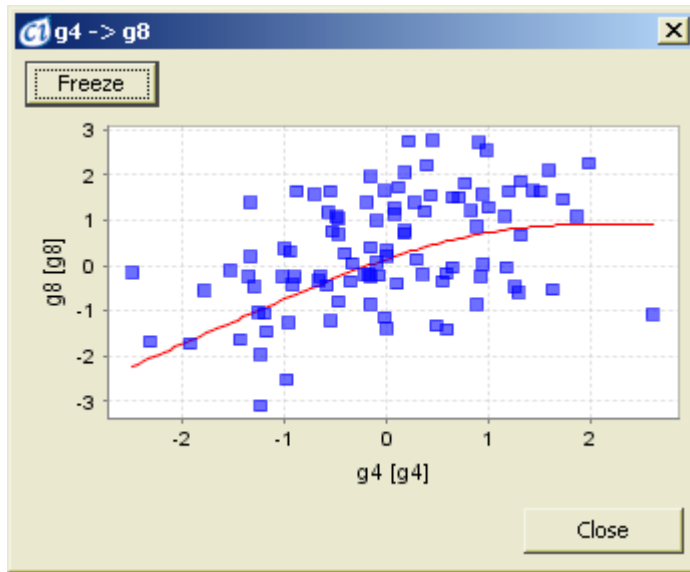
This dialog visualizes the partial residual plot for a selected edge. The partial residual plot is an improved version of the expression plot and displays more detailed information about the results of the micro array experiments, which have been executed to obtain this gene network.

Note: The expression plot is specific for the GNI technology of generating gene networks. The plot requires additional micro-array experiment data. Without this data the expression plot cannot e viewed.

The partial residual plot requires:

- o the bspline data stored in edge comments

- o expression plot file with additional experimental data that is not included in the gene network file.

To view the partial residual expression plot:

1. Make sure that the expression plot file is available in CI.

    For this, open the Preferences dialog box and check that the Expression Plot File location is correctly defined in the Expression Plot section.

2. Select an edge on the canvas.

3. Choose Analyze | Partial Residual Plot from the menu or the Partial Residual Plot icon from the right side toolbar

4. Press the Freeze button to keep the selected plot

5. Select another edge to view its partial residual plot.

17 Gene Mining

This dialog box displays the detailed information concerning the selected genes retrieved from the PubMed, KEGG and MIM databases. You can extract this information either for a selected subset of genes or for all the genes in the network.
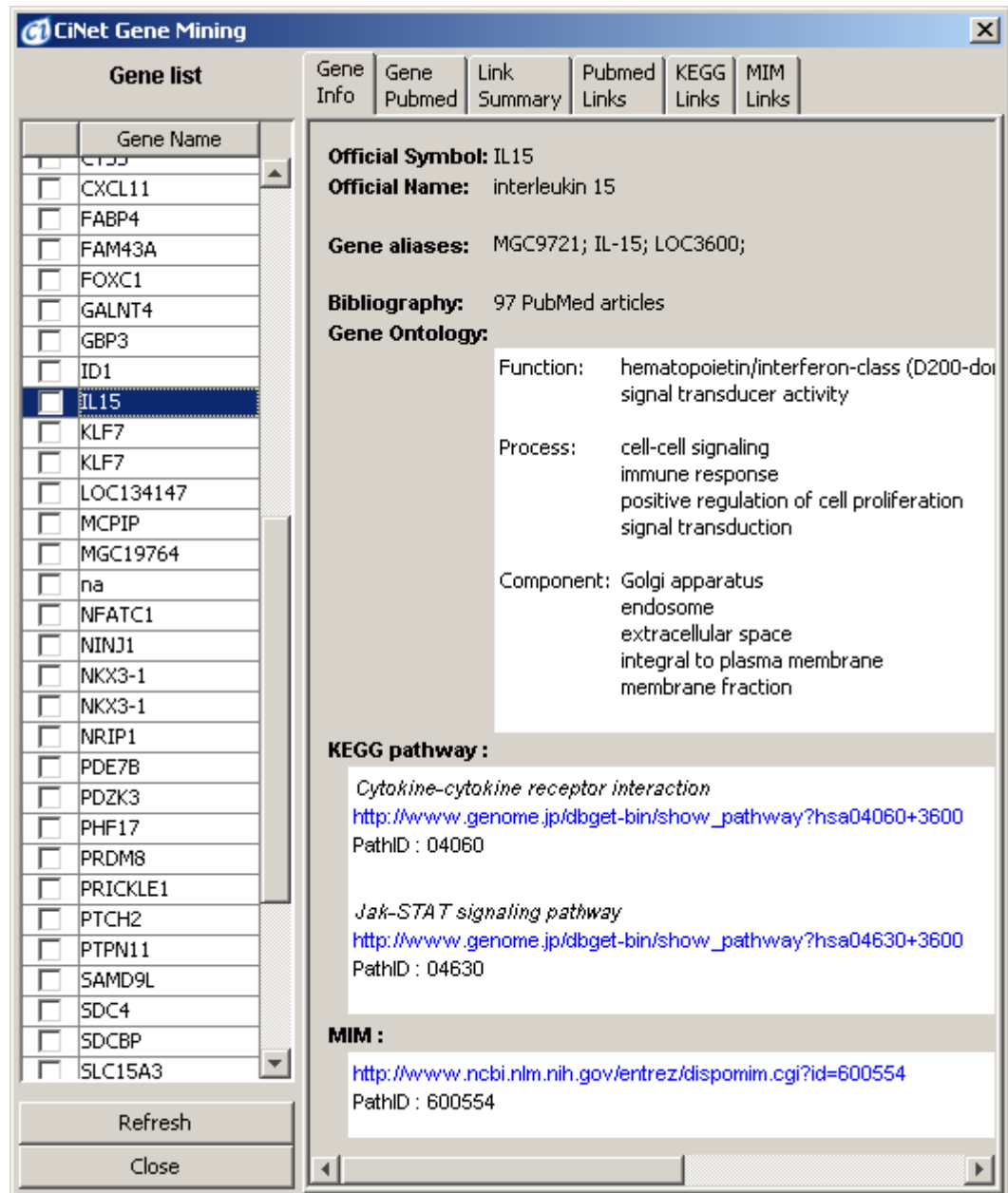
The set of genes upon which gene mining is performed depends on the canvas selection at the time of the execution of the Analyze | Gene Mining command in the following way:

a.   if a gene subnetwork exists on the canvas, then gene mining is performed upon the genes of this subnetwork

b.   otherwise, if the normal selection is not empty then gene mining is performed upon the set of selected genes

c.   otherwise, if none of genes in the network is selected, the gene mining is performed on all genes in the network.

17.1 Gene List

Gene Mining searches for articles concerning selected genes and for links between these genes. The set of genes that has been analyzed in Gene Mining is displayed in the Gene List panel. Selecting a gene in this list, displays the information about this gene in the following described six panels:

17.2 Gene Info

Displays the main information about the gene selected in the Gene List: gene name, official name, aliases and number of PubMed articles, gene ontology, information about gene functions, processes and components

If information about an MIM or KEGG Pathway is present for the selected gene, you may click on the hyperlink to open it in the web browser.

A gene can be represented by its official symbol or an alternate symbol (alias) on the canvas. The symbol used on the canvas is highlighted in blue and underlined in the Gene Info panel. Clicking on it opens detailed information about this gene symbol from Entrez Pubmed database in the web browser.

This information is especially useful when the gene alias is used on the canvas. In such cases you can check in the Entrez Pubmed database, whether the gene alias is unique or ambiguous. If it is ambiguous, the Entrez Pubmed database displays you all possible official symbols for this gene alias.

17.3 Gene Pubmed

In this panel you can observe the Pubmed article list concerning the selected gene. Each article includes the following details: authors, title, journal and publication date. You may also display the article abstracts by selecting the checkbox of each article.

17.4 Link Summary

For a selected gene, this tab lists all related genes in the analyzed set as well as the number of PubMed, KEGG and MIM identifiers that the gene has in common with other genes in the analyzed set.

17.5 PubMed Links

For a selected gene, this tab lists Entrez PubMed entries that link this gene to one or more genes in the analyzed set. You can expand each entry to see the full abstract. The list of related genes is displayed next to each link.

17.6 KEGG Link

For a selected gene, this tab lists KEGG pathways that link this gene to one or more genes in the analyzed set. The list of related genes is displayed next to each link. Click on the http link to access the WWW site with information on a particular MIM identifier.

17.7 MIM Links Panel

For a selected gene, this tab lists MIM identifiers that link this gene to one or more genes in the analyzed set. The list of related genes is displayed next to each link. Click on the http link to access the WWW site with information on a particular MIM identifier.

Note: You may use the shortcut keys Tab and SHIFT+Tab to navigate between the panels. The Tab key switches you one panel forward (to the right), while SHIFT+Tab one panel backward (to the left).

17.8 Refresh Button

This button starts the gene mining process for the selected subnet on the active canvas. It has the same meaning as the Analyze | Gene Mining command.

18 Print Model
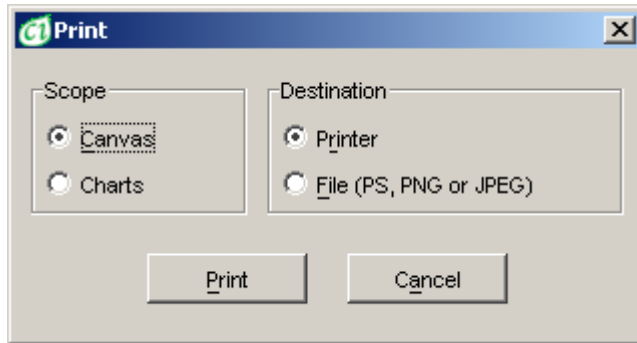
In the Print Model window, you can select the type of data to print and the destination for the print output. Either the model diagram or expression and partial residual plots can be printed. The output can be sent to the printer or to an image file on a disk in PostScript, PNG or JPEG format.

When *Printer* is selected, clicking on the *Print* button opens the *Print* dialog box. In this dialog, you can set the details of the Print job, e.g., the target printer from a list of available printers, the page size, orientation and the margin size.

When the *File* option is selected, clicking on the *Print* button opens the *File Save* dialog box. There you can select the desired file format (PostScript, PNG or JPEG) and the file name. Printing to a PostScript file is completed using the service provided by your default printer. The quality of the output PostScript file depends on your printer setup. PostScript files created on computers connected to different printers might differ.

19 External References
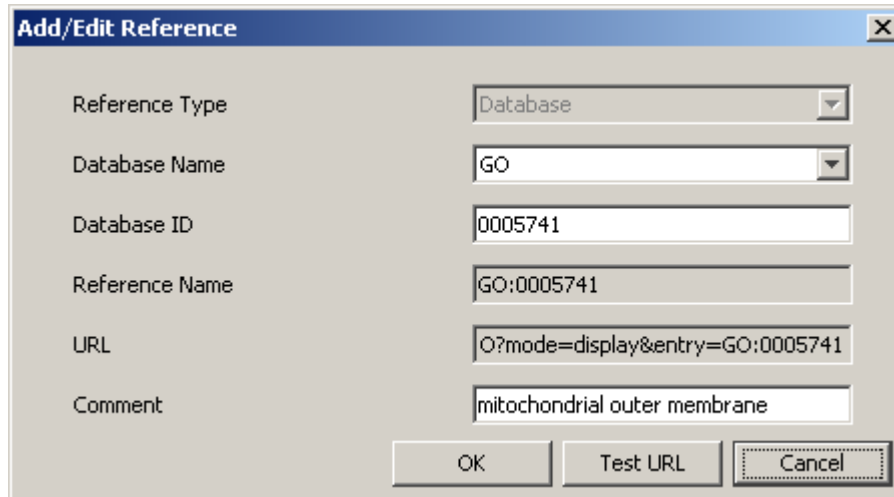
With this dialog you can:
- create new references for the selected element
- edit/remove existing references
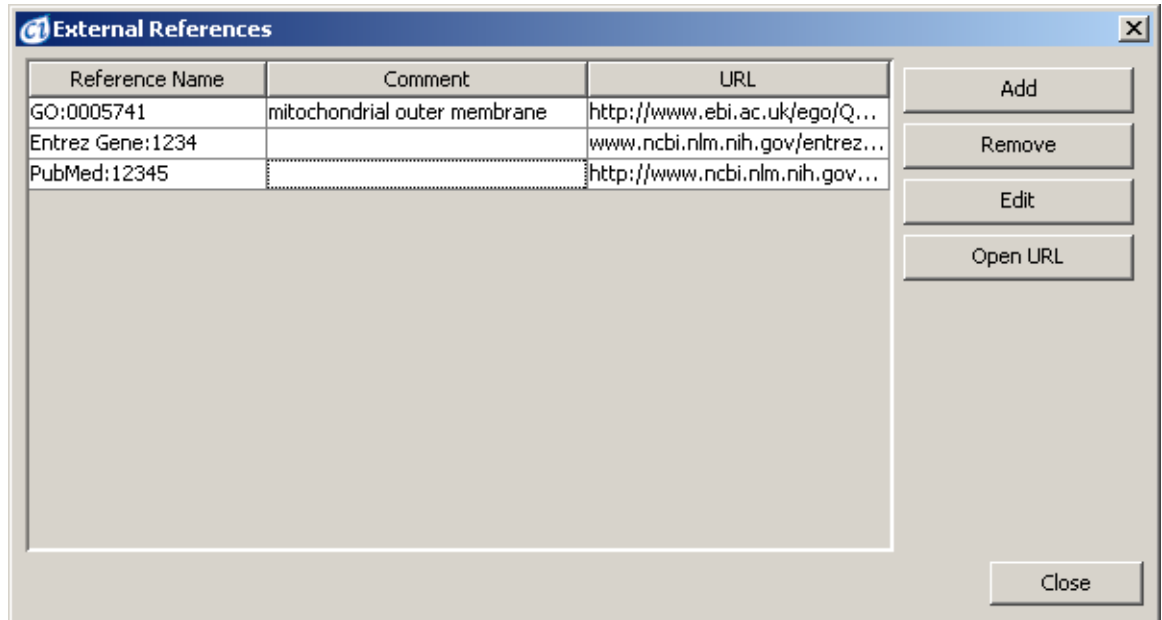
- *External References* is a modeless dialog box that displays the list of references associated with the currently selected element.
- *Add*, *Edit* opens the Add/Edit References Dialog Box, in which you can specify the details of the reference
- *Open URL* opens the URL of the selected external reference in the web browser application
- The reference table displays the reference details in 3 columns: Reference Name, Comment and URL. You can edit any of those reference details by double clicking on the desired table cell.
- For database and publication references, the name and URL is generated automatically when the reference is defined. In some cases you might want to change the default name or URL, e.g. by adding a special, non-default parameter to the URL. Therefore editing of cells in the table is useful for the refinement of automatically generated URL and name attributes.
- Depending on the reference type, the comment property can be used for various purposes. E.g. for it can be the term that is defined by a vocabulary reference, or it ca be a description of the relationship between the element and the reference.
- The database and publication references can be viewed/edited in two dialog boxes External References Dialog Box and in the *Biological Panel* of the Element Settings Dialog Box.

20 Add/Edit References

This modal dialog box enables you to create a new references to an external resource or to edit an existing one, by specifying the reference type and attributes.

- In *Reference Type* combo box you may select one of the available types: *Database*, *Publication* and *Simple*. The *Reference Type* is disabled, if the reference is opened for editing.
- For the *Simple References* you specify the *Reference Name, URL* and optionally the *Comment*. The attributes *Database Name* and *Database ID* are meaningless for simple references.
- For the *Database and Publication References* you specify the *Database Name Database ID* and optionally the *Comment*. The attributes *Reference Name* and *URL* are generated automatically basing on the Database Name and ID. The automatically generated attributes can be modified by the user in the External References Dialog Box
- *Test URL* opens the URL in the web browser application, which allows you to test whether the defined or generated URL is correct.
- Depending on the reference type, the comment property can be used for various purposes. E.g. for it can be the term that is defined by a vocabulary reference, or it ca be a description of the relationship between the element and the reference.

21 Save Dialog
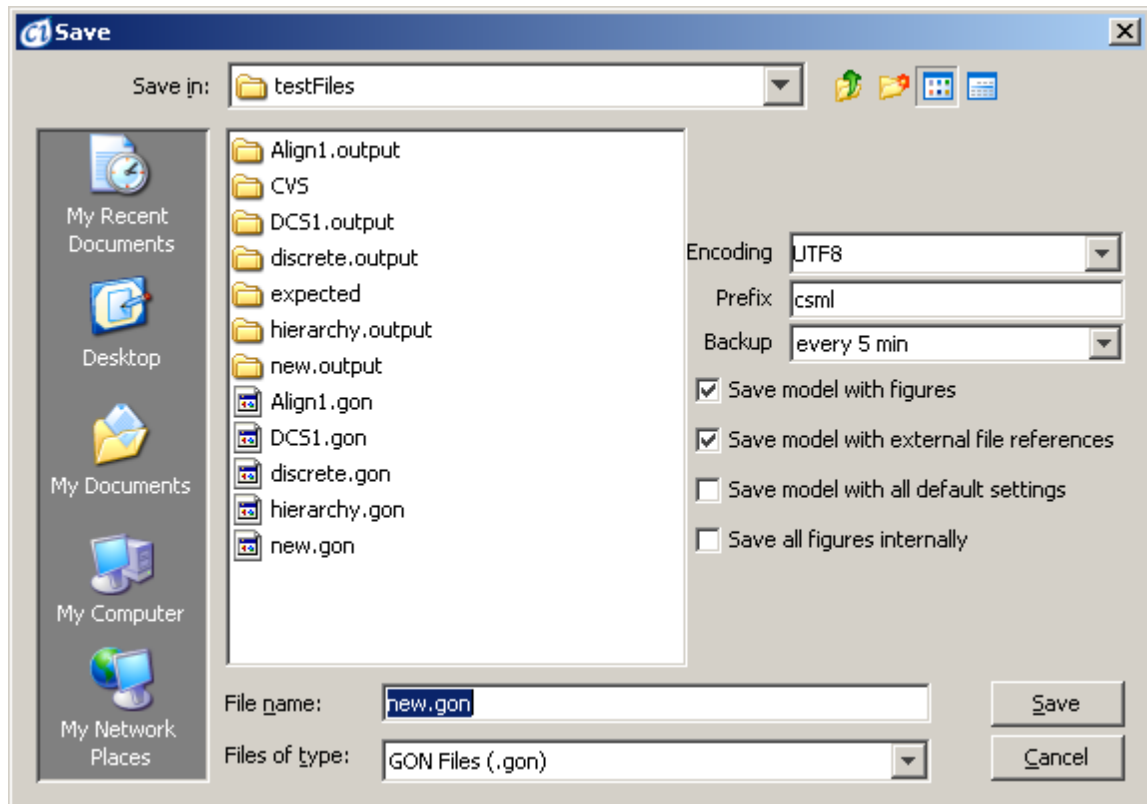
The Save dialog allows the saving of a model in an active canvas window to a file. The dialog has several options:
- *Encoding* determines the file encoding standard.
- *Prefix* specifies the prefix used in all XML tags in the file. The default value csml stands for "Cell System Markup Language".
- If *Save net with figures* is not checked, the data on the position of model elements and their graphical representation will not be written in the file.
- If *Save net with external file references* is checked, the model that makes use of elements in other files will store references to those files. Otherwise, the contents of referenced files will be in included in the output file.
- If *Save net with all default settings* is checked, each element in the canvas will be annotated with the current graphics settings. Use this option when you want to preserve the way the model looks when passing it to a user who may have different display settings.
- If *Save all figures internally* is checked, all images on the canvas will be saved inside the model CSML file. Use this option when you want to include all graphical files (JPEG, PNG, and SVG) inside your model file. This can be useful if you want to pass your model to another user. This will assure that the user will see all the graphics you have added to your model from the external files.

22 About Cell Illustrator

About Cell Illustrator is a modal dialog that contains four tabs: *Version, License, Serial Number* and *3rd Party Components*.

- *Version* contains the version number and the copyright information.
- *License* leads to the End User License Agreement text from the license file.
- *Serial Number* sheet displays the license serial number and the customer data contained in the license file.
- *3rd Party Components* sheet displays information about software components used in Cell Illustrator.