J-Pathway Browser & Viewer Tool

User Manual

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1. Pathways System – Pathway Visualization Tool

Living organisms behave as complex systems that are flexible and adaptive to their surroundings. At the molecular level, organisms consist of intricate networks of molecular reactions, which are often called “biochemical pathways”. In order to maintain, visualize, and ultimately analyze organism functions that result from biochemical pathways, the Pathways System is being developed. The system contains a pathways database and the associated tools to store, compare, query, and visualize biochemical pathways. The aim is to develop an integrated database, and the associated tools to support computational analysis and visualization of biochemical pathways. The ultimate goal of the system is to describe, utilize and predict systems functions and behaviors of living organisms. As of July 2004, the components that the project is comprised of are as follows:

- Pathway Browser (Windows and .Net)
- Pathway Viewer, including Genome Viewer (Windows and .Net)
- Pathway Editor (Windows and .Net)
- Pathway Explorer (Windows and .Net)
- J-Pathway Viewer (Unix, Macintosh, Windows, and Java)

To better understand the chemical interactions taking place in nature, biologists need mechanisms to visualize pathways and processes. Towards this goal, a graphical interface is developed, which allows formulating queries using graphical icons as well as visualizing query outputs in the form of graphs in various abstraction levels. For example, the user can have a pathway graph drawn, showing as many details as he/she chooses. Or, the user can have a pathway graph showing the inter-connections of different pathways where some pathways may be abbreviated as nodes, as opposed to sub-graphs. The goal of the pathway visualization is to facilitate data discovery by providing a robust collection of visualization capabilities.

This user manual describes the J-Pathway Browser and the J-Pathway Viewer. The J-Pathway Browser Tool is a tool that hierarchically lists the pathways, processes, and molecular entities in the database, and allows users to (a) view textual information, and (b) launch the J-Pathway Viewer that visualizes pathway graphs.

The J-Pathway Viewer of the Pathway System provides a visual interface to biochemical pathways stored in the underlying database. The Pathway Viewer is basically a graph drawing and manipulation tool. J-Pathway Viewer provides an intuitive and highly visual means for biochemists to study, query, and curate biological pathways. The tool supports ad-hoc querying of the pathways data as well as menu-driven queries.

1.1 Intended Audience

Any user of the Pathways System is a good candidate for reading this document. There are primarily two classes of users of the system: life scientists (biologists, chemists, and the like), and computer scientists.
All readers will learn how to use J-Pathway browser and viewer from the simple explanation in this user manual. Moreover, the background and the definitions of some of the biology terms used in this system make it easier for the computer scientists to understand the pathway system.

2. Metabolic Pathway Visualization Design

A metabolic pathway consists of multiple processes connected together. A process is any reaction involving molecular entities, and has zero (i.e., a non-enzymatic process) or more catalyzing enzymes, one or more substrates and products, zero or more co-factor-ins, co-factor-outs, inhibitors, or activators. A sample process, drawn with our implementation, is shown in figure 2.1.

![Figure 2.1. A process and its associated molecular entities](image)

The process is visualized in a subgraph composed of nodes representing substrates, products, co-factor ins, co-factor outs, inhibitors, activators, regulators, and a label node, which represents the catalyzing protein of that process, and edges for interactions. Edges can be in many shapes depending on the type of the interaction; for example, arrow-edges means reaction from/to substrates or products, curve-edges are cofactors, T-shape edges represents inhibitor, etc.

In figure 2.1, the substrates of the process are indicated by the pink node(s) at the left; products are indicated using circular purple node(s) at the right. The yellow and orange circle shaped nodes on the top indicate cofactor-ins and cofactor-outs respectively. The light-blue node(s) on the bottom left hand side indicate inhibitors; the dark-blue node(s) on the bottom right hand side indicates activators of the process; and the blue node(s) indicates regulators. The catalyzing protein is indicated using a square shaped node at the center of the process.

All substrate and product nodes are generally visualized only once (green nodes in figure 2.2) in the metabolic pathway graph. However, there are some common molecules (e.g. H2O, O2, etc.) which occur many times in the pathway. Drawing these molecules only once causes multiple cross-edges among processes, thus increasing the complexity of the graph. Therefore, these common molecules are allowed to be redundant in the metabolic pathway graph.
In figure 2.2., green nodes indicate that the nodes are associated with more than one process. In some processes, there is no EC number provided in the pathway database, so the labels of these processes are “No EC#”. If there is more than one EC Number in the process, all EC numbers are visualized, and each of them is separated by a comma (see figure 2.3).

Figure 2.3. Multiple EC numbers in one process

3. J-Pathway Browser & Viewer Architecture

The J-Pathway Browser Tool is a tool that hierarchically lists the pathways, processes, and molecular entities in the database, and allows users to (a) view textual information, and (b) launch the J-Pathway Viewer that visualizes pathway graphs. All data in the tree come from the web services which connect to the pathway database. The J-Pathway Viewer of the Pathway System provides a visual interface to biochemical pathways stored in the underlying database. The Pathway Viewer is basically a graph drawing and manipulation tool. J-Pathway Viewer provides an intuitive and highly visual means for biochemists to study, query, and curate biological pathways. The tool supports ad-hoc querying of the pathways data as well as menu-driven queries. Input data (XML format) may come from web services after the user chooses to view the selected pathway from the J-Pathway Browser, or it may come from the XML file, which was saved by the user, in the user’s local machine. J-Pathway Browser & Viewer can request and receive data from the web services using HTTP post, HTTP get, or SOAP.
Both J-Pathway Browser & J-Pathway Viewer are implemented in Java. Grappa package (http://www.research.att.com/~john/Grappa/) is used and extended to implement the visualization part of the J-Pathway Viewer.

4. J-Pathway Browser Interface

There are three categories in J-Pathway Browser: Pathways, Processes, and Molecular Entities categories.

There are two pop-up menus when right-clicking at each category. For example, by right-clicking at the Pathways category, a user can choose to “Display all pathways” or “Display selected pathways”. The same situation occurs when the user right-clicks at the Processes or Molecular entities category.
By right-clicking at one of the pathway names, the user has two options. First, the J-Pathway Viewer can be launched to display the pathway graph, or the names of all processes involved in this pathway can be displayed in the tree view.
The names of molecular entities involved in a selected process, or the pathway that the selected process or the selected molecular entity involved can be displayed in the same way.

The browser provides the “Queries” menu. There are three querying categories: pathways, processes, and molecular entities. The results of the queries are displayed in tabular formats or in graphical formats. Example queries and results are illustrated in figures 4.6, 4.7, 4.8, and 4.9. Figure 4.6 displays all queries in the processes category. Figure 4.7 shows the dialog box after choosing the option “Expand process”. Figure 4.8 and 4.9 present tabular and graphical results of expanding “Ascorbate 2,3-dioxygenase” process in “Biosynthesis and degradation of ascorbate” pathway in “1” step.
Figure 4.7. Dialog box after choosing “Expand process”

Figure 4.8. The tabular result from the query in figure 4.11

Note: The graphical result: the expanded process is highlighted in red and the result processes are highlighted in blue.

Figure 4.9. “Expand Process” Query Results
5. J-Pathway Viewer Interface

Figure 5.1. J-Pathway Viewer

5.1 Main Menu Options
The J-Pathway Viewer provides the following pull-down menus: (a) File; (b) View; (c) Search; (d) Action; and (e) Help.
Next we discuss each one of these menus.
File menu: The options provided by the “File” menu are shown in Figure 5.2. They include:

(i) Open, which opens the new XML document in the user’s local machine; (ii) Close, which deletes all graphics from this frame; (iii) Save, which saves the pathway graph to the XML document; and (iv) Exit, which closes the frame.

Next we illustrate with examples each of the menu options.
Search Menu: The search options are shown in Figure 5.3. They include:

Figure 5.2. File Menu

Figure 5.3. Search Menu
(i) **Find molecule**, which opens the dialog box containing the names of all molecular entities in the graph. The nodes that have the same molecule name as the selected node name in the dialog box will be highlighted; (ii) **Find process**, which opens a dialog box containing the names of all processes in the graph. The subgraph that displays the selected process in the dialog box will be highlighted;

![Input dialog box for choosing the process name](image)

Figure 5.4. Input dialog box for choosing the process name

(iii) **Find pathway**, which opens the dialog box containing the names of all pathways in the graph. The subgraph that displays the selected pathway in the dialog box will be highlighted; and (iv) **Find splitting nodes**, which opens the dialog box containing the names of all splitting nodes. The nodes that can be split are the ones that are involved in more than one process. The nodes that have the same molecule name as the selected node name in the dialog box will be highlighted.

**View** menu: view menu is shown in Figure 5.6. They include:

![View Menu](image)

Figure 5.6. View Menu

(i) **Zoom in all**, which zooms in all processes in the graph; (ii) **Zoom out all**, which zooms out all processes in the graph; (iii) **Scale to fit**, which changes the size of the displayed pathways graph to fit in the window; and (iv) **Reset zoom**, which sets the size of the graph to the starting size.

**Action** menu: Options provided under “Actions” menu are shown in Figure 5.7. They include:
(i) **Collapse All**, which collapses all processes in the pathways; every node in each process subgraph (the substrates and products, which are inside each process, activators, inhibitors, regulators, cofactor-ins, cofactor-outs and catalyzing protein nodes) is replaced by a single node;

(ii) **Expand All**, which expands all processes in the graph, showing all molecules in each process. (iii) **Show processes’ boxes**, which shows the scope of each process in the graph;
(iv) **Hide processes’ boxes**, which hides the scope of each process in the graph; (v) **Hide all regulators**, which hides all the regulators (activators, inhibitors, regulators) in the graph; (vi) **Display all regulators**, which returns all the regulators in the graph; (vii) **Hide all cofactors**, which hides all the cofactors (cofactor ins, cofactor outs) in the graph; (viii) **Display all cofactors**, which returns all the cofactors in the graph, (ix) **Iconize all processes**, which reduces the sizes of all processes in the graph

(x) **Un-iconize all processes**, which returns all the processes in the graph to the normal sizes; (xi) **Fold selected**, which groups some part of the pathway to a single node
Figure 5.12. After folding the highlighted processes

(xii) **Unfold selected**, which returns the part of the pathway that was folded in the selected node; (xiii) **Unfold all**, which unfolds all nodes; (xiv) **Show all common molecules**, which displays all common molecules that appears in the viewer;

![Message](image)

**Figure 5.13. Common molecule**

(xv) **Add a new common molecule**, which adds a new molecule to the list of the common molecules. The node representing this molecule is split to the substrates or products node;

![Molecular Entities](image)

**Figure 5.14. The dialog box containing all molecules that are not the common molecules**
Remove a common molecule, which deletes the given molecule from a common molecule list and merge all nodes representing that molecule to a single node; (xvii) Find the connecting pathways, which finds pathways that share molecules with the on-screen pathway.
Figure 5.17. Three diamond-shape nodes for three pathways connecting to the given pathway

Figure 5.18. After expanding the connecting pathway in the same window

5.2 Pop-up Menu Options

The pop-up menu is displayed after right-clicking at the selected node, edge, or subgraph in the main active window. The user must left-click first to select the element in the graph and then right-click to activate the pop-up menu.

5.2.1. Pop-up Menu when right-clicking at the process subgraph
This menu includes (i) **Zoom In this process**, which zooms in the selected process; (ii) **Zoom Out this process**, which zooms out the selected process, (iii) **Rotate**, which rotates this process. The user can enter the rotation angle in degrees in the rotation dialog box. Positive degree means clockwise rotation. Negative degree means counterclockwise rotation.

(iv) **Iconize this process**, which changes the selected process to the iconized state.
If the process is in the iconized state, the pop-up menu is changed from “Iconize this process” to “Un-iconize this process”.

The full process will be displayed after clicking at the “Uniconize this process”.

(v) **Collapse this process**, which collapses the selected process to a single node;

If the process is collapsed, the pop-up menu is changed from “Collapse this process” to “Expand this process”.
The process will be expanded after clicking at “Expand this process” menu.

5.2.2 Pop-up Menu when right-clicking at the catalyzing protein node

This menu includes:

(i) **Zoom In this process**, **Zoom out this process**, **Rotate**, and **Collapse this process** are the same as those explained above; (ii) **Queries**, which shows the query results that is related to the selected catalyzing protein or process;

(iii) **Toggle name**, which hides/unhides node labels in the selected process;
(iv) **Change EC to name**, which changes the label at the catalyzing protein node from EC to the process name;

If the catalyzing protein node shows the name of the process, the pop-up menu is changed from “Change EC to Name” to “Change Name to EC”.

(v) **Properties**, which will be explained in the next section.

### 5.2.3 Pop-up Menu when right-clicking at the node

This menu includes:
(i) **Queries** – the same as explained above, (ii) **Properties** – Changes the properties of the selected node, or applies the changes to all substrates, all products, all cofactor-ins, all cofactor-outs, all inhibitors, all activators, all regulators, all catalyzing proteins, or all nodes. Node properties include:

- color – the node color
- style – the node style (filled or normal)
- shape – the node shape, such as square, circle, house, etc.

5.2.4 Pop-up Menu when right-clicking at the node associated with more than one process

This menu includes:

- **Horizontal Split**, which splits the selected node horizontally;
(ii) **Vertical Split**, which splits the selected node vertically; (iii) **Manual Split**, which splits the selected node manually (press ctrl + left click at the edges). All the split nodes will be drawn at the same position after splitting; (iv) **Merge Splitting nodes**, which merges the splitting nodes into one node (press ctrl + left click at the nodes). The nodes that can be merged are the ones that represent the same molecule only.

### 5.2.5 Pop-up Menu when right-clicking at the edge

![Figure 5.37. Edge menu](image)

(i) **Change to straight line** – Changes the selected edge to the straight line;  
(ii) **Properties** – Changes the properties of the selected edge or apply the changes to all edges. Edge properties include:

- color – the edge color
- style – the edge style (solid, dashed, or dotted)
- thickness – the edge thickness

![Figure 5.38. Edge properties dialog box](image)
5.2.6 Pop-up menu when right-clicking at the control point node

When clicking at an edge, all the control points (the bending points) of that edge are shown. That control point can be removed by right-clicking at the control point and choosing “Delete Control Point”.

5.3. Other functions

Other functions include: (i) **Moving a node**: The node can be moved by dragging the node; (ii) **Moving a process**: The process subgraph can be moved by dragging the catalyzing protein node; and (iii) **Changing an edge to the curve**: When clicking at the edge, the new control point will be created. By dragging the control point, the edge will be changed to the curve.
Figure 5.42. The curve