

Drawing pathways using PathWhiz

Overview:

PathWhiz contains 6 main element types:

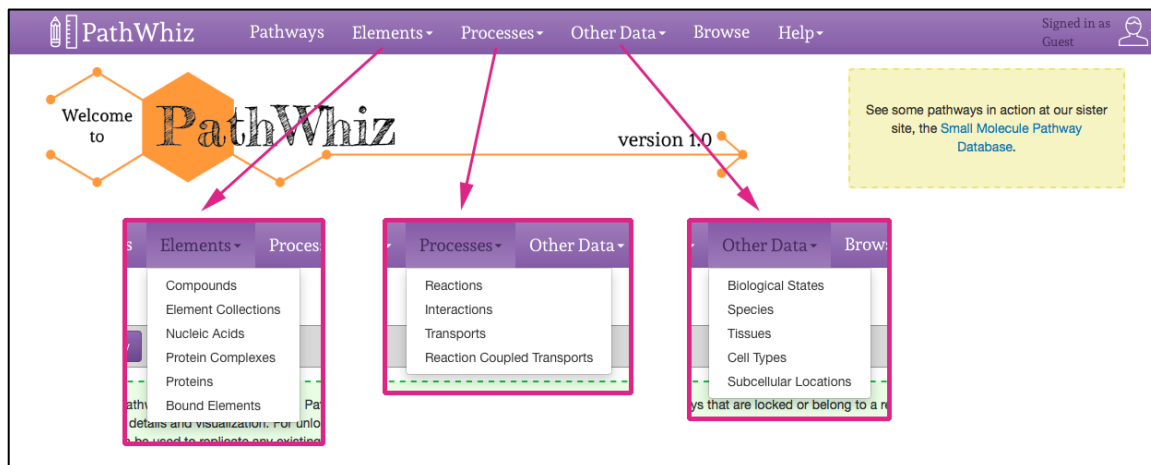
- **Compound:** A small molecule
- **Protein:** An amino acid macromolecule, corresponding to a singular entry in UniProt
- **Protein Complex:** A combination of one or more proteins, along with any modifications and cofactors
- **Nucleic Acid:** DNA or RNA
- **Element Collection:** Represents a general class of compounds, proteins complexes, or nucleic acids (i.e. alcohols, bacterial ribosomes, etc.)
- **Bound Element:** A protein complex or nucleic acid bound to one or more compounds, protein complexes, elements collections, or nucleic acids

And 4 main process types:

- **Reaction:** Contains at least one left and right element, and zero or more enzymes
- **Reaction Coupled Transport:** Contains at least one left and right element with their respective biological states, and zero or more enzymes
- **Transport:** Contains up to three elements that are transported simultaneously and zero or more transporters
- **Interaction:** Contains two elements where the first either activates or inhibits the second

Some elements also have an associated Biological State, indicating the biological location where it's found (in the context of the pathway).

All elements and processes can be browsed via the PathWhiz menu bar:



You can also add your own elements and processes if needed. When adding new elements to the database, required fields are marked with a red *.

PathWhiz Pathways Elements Processes Other Data Browse Help Signed in as Guest

New Reaction

Required fields are marked with a *

Left Elements + Add Left Element
** Must have at least one left element*

Stoichiometry* 1 ✖

Element Type* Compound

Element Name* Pyruvic acid New

Stoichiometry* 1 ✖

Element Type* Compound

Element Name* L-Glutamic acid New

Direction

→

Spontaneous? Yes No Unknown

Right Elements + Add Right Element
** Must have at least one right element*

Stoichiometry* 1 ✖

Element Type* Compound

Element Name* L-Alanine New

Stoichiometry* 1 ✖

Element Type* Compound

Element Name* Oxoglutaric acid New

Enzymes

Enzyme* Alanine aminotransferase 1 (Homo sapiens) New ✖ Remove

EC Number* 2.6.1.2

+ Add Enzyme

✓ Create Reaction ✖ Discard

Check out the legend (<http://smpdb.ca/pathwhiz/legend>) to see what the different elements look like.

Quick Start Guide

Creating a new pathway:

Pathways

+ New Pathway Upload Pathway Search

This index can search and filter all of the pathways currently in Pathwhiz. Pathways that are locked or belong to a registered user can be viewed and replicated but not edited. Use the **Show** button to view the pathway details and visualization. For unlocked pathways, use the **Edit** button to change the pathway details and the **Draw** button to change the visualization. The **Replicate** button can be used to replicate any existing pathway so that it may be edited and saved as a new one.

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PW ID	Name	Type	Species	Last Updated	Creator					
PW000751	2,3-dihydroxybenzoate biosynthesis	Metabolic	Escherichia coli	2015-3-30	miguel ramirez	Show	Registered user's pathway	Replicate		
PW000656	3-Methylthiofentany Pathway	Drug	Homo sapiens	2015-2-8	Public User: Anonymous	Show	Edit	Draw	Destroy	Replicate
PW000714	Abacavir Pathway	Drug	Homo sapiens	2015-2-8	Public User: Anonymous	Show	Edit	Draw	Destroy	Replicate
PW000291	Abciximab Pathway	Drug	Homo sapiens	2015-3-30	Public User: Anonymous	Show	Locked pathway	Replicate		
PW000364	Acebutolol Pathway	Drug	Homo sapiens	2015-2-8	WishartLab	Show	Registered user's pathway	Replicate		
PW000312	Acenocoumarol Pathway	Drug	Homo sapiens	2015-2-8	WishartLab	Show	Registered user's pathway	Replicate		
PW000687	Acetaminophen Pathway	Drug	Homo sapiens	2015-2-8	Public User: Anonymous	Show	Edit	Draw	Destroy	Replicate
PW000616	Acetaminophen Pathway	Drug	Homo sapiens	2015-2-8	Public User: Anonymous	Show	Edit	Draw	Destroy	Replicate
PW000128	Acetylsalicylic Acid Pathway	Drug	Homo sapiens	2015-3-25	WishartLab	Show	Locked pathway	Replicate		
PW000725	Activation of cAMP-dependent protein kinase, PKA	Signaling	Homo sapiens	2015-2-8	Yilu Su	Show	Registered user's pathway	Replicate		

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If you're not there already, launch the drawing system by selecting "Draw" from the menu bar of the PathWhiz home page (this may take a minute to load), and go to the pathways index via the "Pathways" link. Here you can search, filter and view all the pathways currently in PathWhiz. If you are a guest user, you will be able to edit all other public pathways. If you log into your own account, you can only edit your own pathways. These can be filtered using the "My Pathways Only" checkbox.

NOTE FOR GUEST USERS: When using PathWhiz as a guest, any pathways you create will be public and can also be accessed and altered by other guest users. To create your own private pathways that can't be edited by other users, sign up for your own account. It's free!

To create a new pathway, use the “New Pathway” button on the top left and enter your pathway details. Required fields are marked with a red *.

The screenshot shows the 'New Pathway' form in the PathWhiz application. The form is titled 'New Pathway' and includes a navigation bar at the top with 'PathWhiz' and menu items: 'Pathways', 'Elements', 'Processes', 'Other Data', 'Browse', and 'Help'. The user is signed in as 'Guest'. The form contains several sections:

- Name** (required): A text input field with the placeholder 'e.g. Alanine Metabolism'.
- Type** (required): A dropdown menu.
- Species** (required): A search input field with the placeholder 'Search species, e.g. Homo sapiens' and a 'New' button.
- Guest Identifier** (optional): A text input field with the placeholder 'e.g. a name/pseudonym or email'.
- Description** (optional): A large text area with the placeholder text: 'You can describe what your pathway is about here, e.g. Alanine is most commonly produced by the reductive amination of pyruvate via alanine transaminase. This reversible reaction involves the interconversion of alanine and pyruvate...'
- Private?** (optional): Radio buttons for 'Yes' and 'No', with 'No' selected.
- Create From Pathway** (optional): A text input field with the placeholder 'Search pathways, e.g. Alanine Metabolism'.
- E value** (optional): A text input field with the placeholder '1e-10'.
- References** (optional): A section with an '+ Add Reference' button and two buttons at the bottom: '✓ Create Pathway' and '✗ Discard'.

A red asterisk (*) indicates required fields. A red note at the bottom of the form states: '* If you are importing a pathway from a different species, PathWhiz will BLAST UniProt to try and find protein homologs if the protein has not been yet been mapped to the specified species in the PathWhiz database. This can take several minutes. In addition, if you are converting from a Eukaryotic species to a Prokaryotic species, PathWhiz will infer which images and label to remove.'

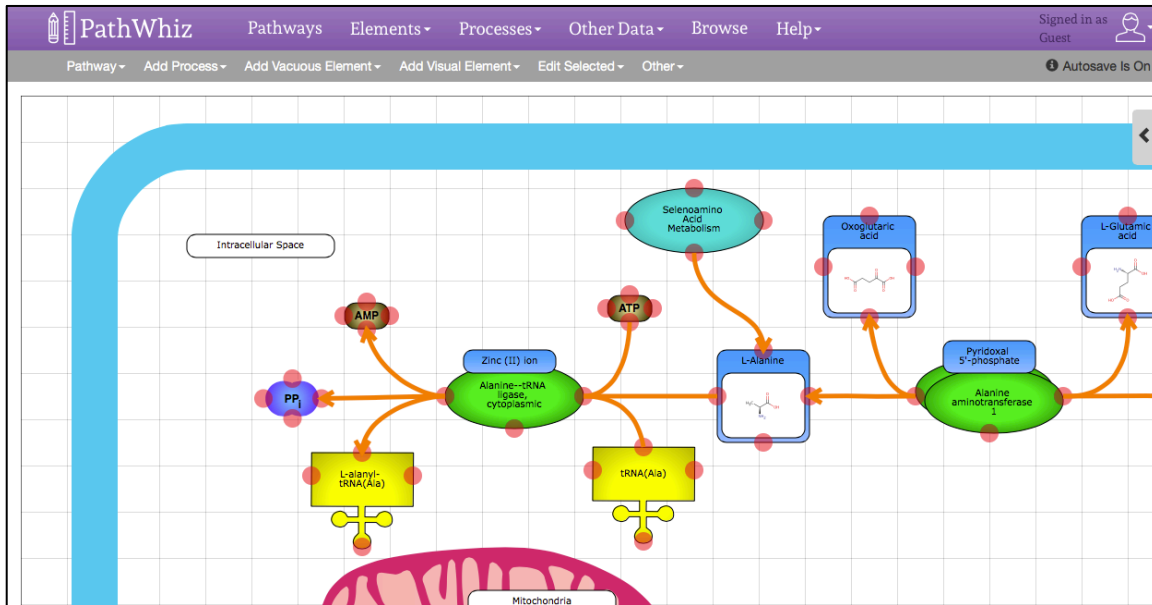
The name, type, and species are required fields. A private pathway means other users will not be able to see it.

Filling out the “Create From Pathway” and “E-value” fields will generate the basis of your pathway from an existing pathway in the database. The E-value is used by BLAST to find protein homolog if the species is different. Leave these blank if you wish to start from scratch.

Once your pathway has been created, you will be taken to the pathway drawer.

Using the pathway drawer:

Once your pathway has been created, the visualization editor can also be accessed from the Pathway index via the “Draw Pathway” button.



Adding Processes/Elements: To add new elements, use the “Add Process”, “Add Vacuous Element” and “Add Visual Element” links in the menu bar. When adding processes, you will be prompted to either select existing processes from the database or create your own. Search the database by entering text into the associated text box. Once you’ve selected a process and added its details, the “Create” button will add it to the visualization. Vacuous and Visual elements are added directly to the visualization, and can then be edited.

Add Reaction

Reaction

L-Alanine + Oxoglutaric acid ↔ L-Glutamic acid + Py...

Biological State

Homo sapiens, Cell, Mitochondrial Matrix

Enzymes

Alanine aminotransferase 1 (Homo sapiens)

Render Options

Left to Right

Moving Elements: Click and drag elements to move them around. Multiple elements can be selected using single clicks. Elements selected for moving are highlighted in red. Unselect them by clicking on them a second time.

Snap Points: Snap points on elements are indicated by red circles (these do not appear in the final visualization). To snap an edge to an element, double click to select the desired edge. Then click the end point you wish to snap (indicated with a grey circle), followed by the snap point of the element you wish to join it to.

The screenshot displays the PathWhiz software interface. The main window shows a metabolic pathway diagram with various molecules and enzymes. A central green oval represents 'Alanine--tRNA ligase, cytoplasmic', which is connected to 'Zinc (II) ion', 'AMP', 'ATP', 'L-Alanine', 'L-alanyl-tRNA(Ala)', and 'tRNA(Ala)'. The 'L-Alanine' molecule is highlighted with a red border and a dotted line, indicating it is selected for editing. The 'Edit Selected' sidebar on the right shows the following settings for L-Alanine:

- Update visualization automatically:**
- Template:** Small Compound Visualization
- Biological State:** Homo sapiens, Cell, Cytosol
- New Biological State:** (empty)
- Z-Index:** 10 (with Move up and Move down buttons)
- Component of:**
 - Adenosine triphosphate + L-Alanine + tRNA(Ala) → Adenosine monophosphate + ...
 - L-Alanine + Oxoglutaric acid ↔ L-Glutamic acid + Pyruvic acid (Homo sapiens)
 - Selenoamino Acid Metabolism

Editing Elements: Double click on an element to select it for editing. The selected element will be encased by a dotted line. Once an element is selected, the “Edit Selected” menu item and sidebar will become active. On the sidebar you can edit the appearance of individual elements, including the template used and z-index. On the “Edit Selected” menu or bottom of the sidebar, processes and complexes that this element belongs to can be accessed, edited, and re-rendered.

A NOTE ABOUT THE SIDEBAR: Changes made on the sidebar will appear automatically. As this may slow performance on larger pathways, automatic updating can be turned off using the “Update visualization automatically” checkbox on the top of the sidebar. When off, an “Update” button will appear on the sidebar to allow you to update your visualization manually.

Editing a process (shown below) will allow you to change the templates used for elements and edges. Different templates can be selected by entering text and searching or using the arrow keys to scroll through the choices. Some choices have colors to indicate the color of the visualization. You can also change the z-index (i.e. layer) of the visualization, and hide elements if desired.

Edges can also be double clicked. Selecting an edge lets you modify its end points and curvature. Double clicking on the end point of a selected edge will allow you to cycle through the different kinds of end points.

Edit Reaction

Biological State

Homo sapiens, Cell, Cytosol

Compounds

Compound				Edge			
Name	Template*	Biological State	Z-Index	Hide?	Type*	Z-Index	Hide?
L-Alanine (Left)	<input type="button" value="Small Compo..."/>	Homo sapiens, Cel...	10	<input type="checkbox"/>	<input type="button" value="Catalysis Arrow"/>	18	<input type="checkbox"/>
Oxoglutaric acid (Left)	<input type="button" value="Small Compo..."/>	Homo sapiens, Cel...	10	<input type="checkbox"/>	<input type="button" value="Catalysis Arrow"/>	18	<input type="checkbox"/>
L-Glutamic acid (Right)	<input type="button" value="Small Compo..."/>	Homo sapiens, Cel...	10	<input type="checkbox"/>	<input type="button" value="Catalysis Arrow"/>	18	<input type="checkbox"/>
Pyruvic acid (Right)	<input type="button" value="Small Compo..."/>	Homo sapiens, Cel...	10	<input type="checkbox"/>	<input type="button" value="Catalysis Arrow"/>	18	<input type="checkbox"/>

Element Collections
No Element Collections

Nucleic Acids
No Nucleic Acids

Protein Complexes
No Protein Complexes

Bound Elements
No Bound Elements

Enzymes

Alanine aminotransferase 1

Render Options: The render options under the “Edit Selected” menu will attempt to layout the selected process for you automatically in a horizontal/vertical and right-to-left/left-to-right pattern. Highlighted elements will not be moved.

Combining Processes: Processes can be built onto one another by first highlighting the element you wish to build from, then selecting the desired process from the menu. This will cause your new process to be rendered attached to the existing process. If you’ve highlighted one or more elements before attempting to add a new process, you will only be able to add processes that can be connected to the highlighted elements.

From the “Pathway” menu link you can edit your pathway details, or view and export the pathway visualization (more below).

From the ‘Other Visual Elements’ menu link you can add:

- Membranes
- Images (including cellular components, tissues, organs)
- Labels
- Zoom boxes

From the “Other” menu link you can toggle the drawing grid (grid does not appear in generated images), turn autosave on and off, change the pathway canvas size or fit the canvas to your pathway, import another pathway, clear all the pathway elements, or reset to your last save point (if autosave is off).

A NOTE ABOUT AUTOSAVE: By default, PathWhiz will save your diagram each time you move or edit an element. With larger pathways, this may cause a decrease in performance; if this is the case you may wish to turn off autosave. Note that regardless of whether you have autosave turned on or off, the pathway will be saved whenever an element is added or removed from the visualization. With autosave turned off you can save updates to the pathway using the “Save Pathway” button in the top right corner, or reset the pathway to the last save using the “Reset Pathway” option in the “Other” menu.

Exporting and viewing your pathway:

When you are ready to export and view your pathway, select “Export and View” from the “Pathway” menu link. This will take you to a page showing the pathway details. Click on the green “Generate Image Files” button to export the pathway. You may choose to generate the images with a blue or white background.

The screenshot shows the PathWhiz web interface. At the top, there is a navigation bar with the PathWhiz logo and menu items: Pathways, Elements, Processes, Other Data, Browse, and Help. On the right side of the navigation bar, it says "Signed in as Guest" with a user icon. Below the navigation bar, the main content area is titled "Acetaminophen Pathway". To the right of the title are three buttons: "Edit Details", "Draw Pathway", and "Propagate". Below the title, there are several fields and buttons:

- PathWhiz ID(s):** PW000687
- Last Updated:** February 8, 2015 at 5:05:41 PM MST
- Type:** Drug
- Species:** Homo sapiens
- Creator:** WishartLab
- Description:** The mechanism of action of Acetaminophen is thought to be due to its ability to block prostaglandin synthesis by inhibiting cyclooxygenase 1 and 2 (COX-1 and -2), also called prostaglandin G/H synthase 1 and 2. COX-1 and -2 catalyze the conversion of arachidonic acid to prostaglandin G2 and prostaglandin G2 to prostaglandin H2. Prostaglandin H2 is the precursor to a number of prostaglandins (e.g. PGE2) involved in fever, pain, swelling, inflammation, and platelet aggregation. Acetaminophen antagonizes COX by binding to the upper portion of the active site, preventing its substrate, arachidonic acid, from entering the active site. Prostaglandins have been shown in many animal models to be mediators of certain kinds of intraocular inflammation. In studies performed in animal eyes, prostaglandins have been shown to produce disruption of the blood-aqueous humor barrier, vasodilation, increased vascular permeability, leukocytosis, and increased intraocular pressure.
- Locked?:** No
- Background Color for Images:** Blue (with a dropdown arrow) * If you change the background color, you must (re-)generate the image files for the change to appear
- Images Last Generated:** March 26, 2015 at 4:28:24 AM MDT (with a green "Generate Image Files" button)
- Show in Viewer:** PW000687
- Related Pathways:** Search for Related Pathways (with a search button)

Pathways must be exported before they can be viewed in the database. This process creates the PNG, SVG, BioPAX, SBML, SBGN, and PWML files for your pathway and may take several minutes. Once complete, the time of export will be recorded and a link to your pathway (a purple button with its PathWhiz ID) will appear under "Show In Viewer". Click this button to view your pathway in the interactive PathWhiz Viewer:

The screenshot shows the PathWhiz web interface. The main area displays a metabolic pathway for Caffeine Metabolism. The pathway is shown as a network of chemical structures (metabolites) and enzymes (represented by green circles). The starting point is Caffeine, which is metabolized into three dimethylxanthines: paraxanthine, theobromine, and theophylline. Each of these metabolites is further metabolized into various methyluric acids, which are then excreted in the urine. The pathway is shown in a hierarchical manner, with Caffeine at the top and its metabolites branching out below. The interface includes a search bar, navigation buttons (Browse, Draw, Downloads, Help), and a sidebar with a description, references, and meta-data for the pathway.

Pathway Description

Caffeine Metabolism
Homo sapiens
Metabolic Pathway

Caffeine from coffee or other beverages is absorbed by the stomach and small intestine within 45 minutes of ingestion and then distributed throughout all tissues of the body. Caffeine is metabolized in the liver by the cytochrome P450 oxidase enzyme system (specifically, the CYP1A2 isozyme) into three metabolic dimethylxanthines: paraxanthine, theobromine and theophylline. Paraxanthine increases lipolysis, leading to elevated glycerol and free fatty acid levels in the blood plasma. Theobromine dilates blood vessels and increases urine volume. Theobromine is also the principal alkaloid in cocoa, and therefore chocolate. Theophylline relaxes smooth muscles of the bronchi, and is used to treat asthma. Each of these caffeine metabolites is further metabolized into various methyluric acids and then excreted in the urine.

References

Caffeine Metabolism References

Lehninger, A.L. (2005) *Lehninger principles of biochemistry* (4th ed.). New York: W.H Freeman.

Salway, J.G. (2004) *Metabolism at a glance* (3rd ed.). Alden, Mass.: Blackwell Pub.

Meta Data

Creator: WishartLab
Created On: August 01, 2013 at 13:54
Last Updated: March 24, 2015 at 23:00