

DATAPUNK_

UBCOEGM



QuodLibet

NETWORKING THE VIS

USER GUIDE, VERSION 1.4

[HTTP://WWW.DATAPUNK/QUODLIBET/](http://www.datapunk/quodlibet/)

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WELCOME TO QUODLIBET

*A **quodlibet** is a piece of music combining several different melodies, usually popular tunes, in counterpoint and often a light-hearted, humorous manner. The term is Latin, meaning "whatever" or literally, "what pleases."*

QUODLIBET is a suite of network creation, editing and querying software written by Peter D'Adamo. QUODLIBET is a software application that displays biochemical pathway data in a way that is interactive and information intensive.

In addition to providing information about genetic-protein interactions QUODLIBET also allows for additional information to be harvested, including data on the effects of natural products on gene-protein expression.

Unlike most biochemical pathway/network depiction programs QUODLIBET actually 'thinks' in a social network sense in that it analyzes the network and reports on many graph functions including betweenness centralities, page-ranks, and cluster coefficients. This allows an immediate understand of which nodes are acting in a critically important role in the network.

It was designed to be simple, easy to user and fun to edit and develop in. Because it is web-based, no special software is required, other than a modern browser and a decent Internet connection. QUODLIBET runs under the DataPunk platform and is open-access. Curators can use the extensive editing tools to add to, alter, or create entirely new networks.

QUODLIBET AND NETWORK THEORY

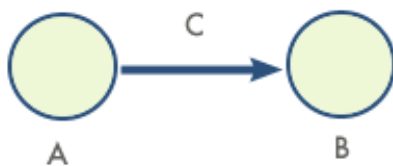
QUODLIBET is designed to utilize a variety of mathematical tools that allow for the design, construction and analysis of metabolic networks. This discipline is referred to a *graph theory*, although the 'graphs' here are not the graphs most of us know from statistics. These of *graphs* are mathematical structures used to model pairwise relations between objects from a certain collection. For example, a map of the NYC subway system could be considered a graph, with the subway stations as the objects and the subway track lines as the relationships.

A *graph* in this context refers to a collection of *nodes* (subway stations) and a collection of *edges* (subway tracks) that connect pairs of nodes. A graph may be *undirected*, meaning that there is no distinction between the two nodes associated with each edge (i.e. a subway train could go either way on the same track; a good thing for some networks, a bad thing for a subway system) or its edges may be *directed* from one node to another (much safer!).

Almost every graph in QUOLIBET is directed, since edges often represent processes such as enzymes or transcriptional activations that are inherently directional. Graphs are represented graphically by drawing a dot or circle for every node, and drawing a line between two nodes if they are connected by an edge. If the graph is directed, drawing an arrow indicates the direction.



A typical node and a directed edge.

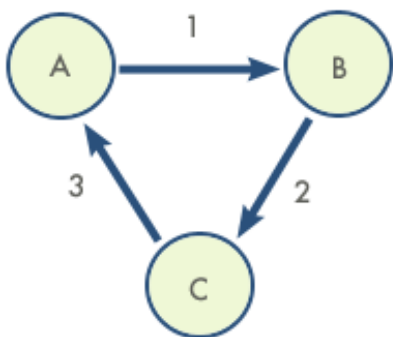


Two nodes (A and B) connected by a directed edge (C).

Node A is typically called the 'source node' and Node B the 'destination node.'

Graphs are among the most commonly used models of both natural and human-made structures. They can be used to model many types of relations and process dynamics in physical, biological and social systems. Many problems of practical interest can easily be represented by graphs.

A graph with weighted edges in the context of graph theory is called a *network*. Network analysis has many practical applications, for example, to model and analyze traffic networks or even analyze social patterns and behaviors.

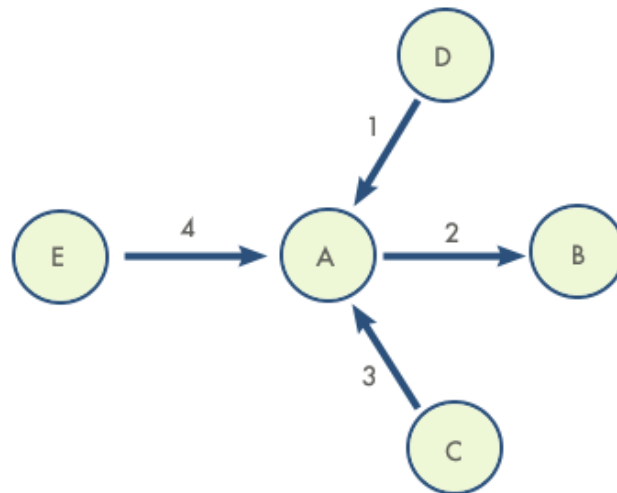


A simple network comprised of three nodes and three edges.

Several functions, including betweenness centrality and PageRank, are used by QUODLIBET to perform various types of analysis on molecular network maps.

Node Degree

For a node, the number of head endpoints adjacent to a node (i.e. nodes that point to this node) is called the *in-degree* of the node and the number of tail endpoints (i.e. nodes that from this node to other nodes) is its *out-degree*. To use a social metaphor, the in-degree of a node representing you in a social network might be the number of people who consider you a personal friend. The out-degree of your node would then be the number of people in the network that you consider a personal friend. Graph theory and human nature both imply that these may well turn out to be very different numbers. A node that has as many incoming edges as outgoing is said to have an *in-degree of zero*.

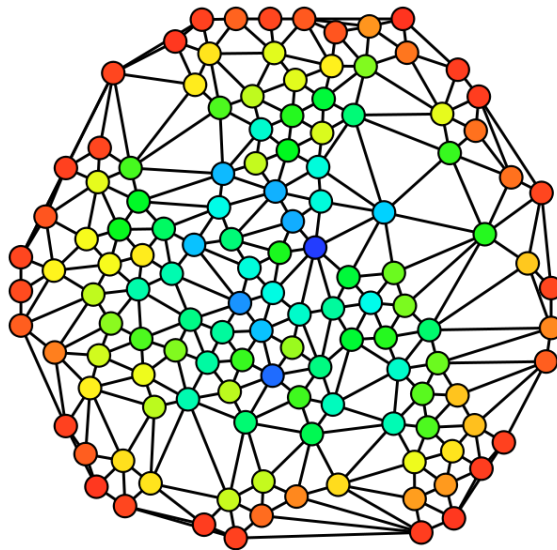


In this small network, Node A has an in-degree of 3 (incoming Edges 1,3,4 from Nodes B,C,and E) and an out-degree of 1 (outgoing Edge 2 to Node B) . Thus its 'degree value' is +2. Node C has no in-degree edges and one out-degree (Edge 3 to Node A). Its degree value is -1.

Node Centrality

Within graph theory and network analysis, there are various measures of the *centrality* of a node within a graph that determine the relative importance of the node within the graph (for example, how important a person is within a social network or how well-used a road is within an urban network).

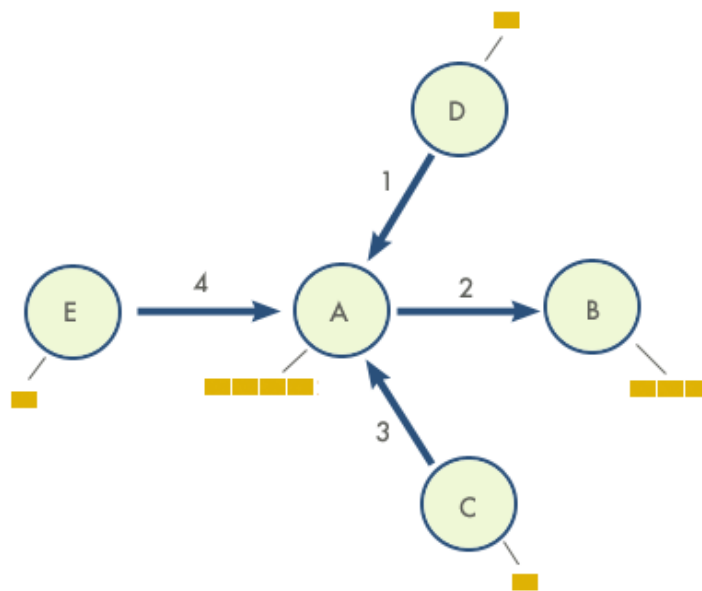
Betweenness centrality is a measure of a node's centrality in a network equal to the number of shortest paths from all vertices to all others that pass through that node. Betweenness centrality is a more useful measure of the load placed on the given node in the network as well as the node's importance to the network than just connectivity.



Betweenness Centrality. Hue (from red=0 to blue=max) shows the node betweenness. Blue colored nodes are highly centralized. Failure of these nodes could lead to serious consequences for the network.

Page Rank

Page Rank is a link analysis algorithm, named after Larry Page (one of the founders of Google) and used by the Google Internet search engine, that assigns a numerical weighting to each element of a hyperlinked set of documents, such as the World Wide Web, with the purpose of 'measuring' its relative importance within the set. Like life, with Page Rank, node importance *is not based on what you know, but who you know*.



Page Rank. Although Node B only has one edge, it has a high Page Rank (symbolized by the yellow power bars) because, the one edge it does possess is incoming from Node A, a very important node in the network.

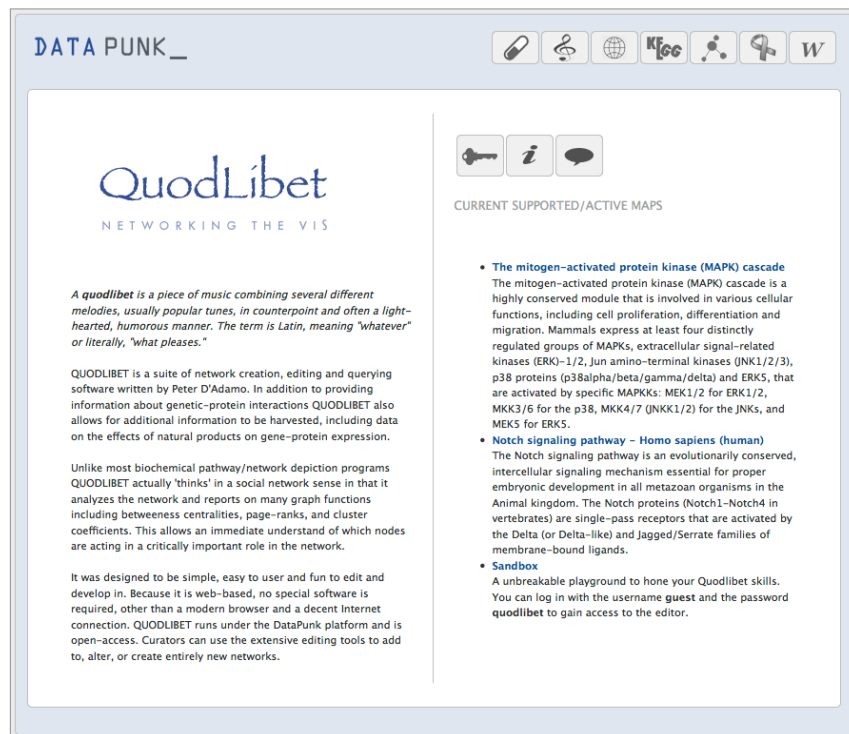
GETTING STARTED

There are a few minimum requirements that need to be met before you can begin using QUODLIBET:

- You will need a modern browser. QUODLIBET draws networks in a special graphic format called SVG (Scalable Vector Graphics). The format allows for some very cool functions, such as the ability to zoom in or out of the network without any loss to the quality of the image. Most current browsers, including the most recent versions of Internet Explorer, Firefox, Safari and Chrome support scalable SVG graphics, however this feature is only available in the most current versions of IE and Safari. QUODLIBET will detect which browser you are using and let you know if it is capable of displaying SVG. We have found that Google Chrome (www.google.com/chrome) and Mozilla Firefox (www.mozilla.org) work well with both Mac and PC computers. Both are free to download.
- You will need to have 'pop-ups' enable on your browser. This is normally the default status on most browsers, unless you are using a 'pop-up killer' program, in which case you will have to create an exception for the QUODLIBET web address (www.datapunk.net/quodlibet/)
- You will need a reasonably decent Internet connection. A cable modem or DSL connection is more than sufficient.
- You will need to allow Javascript to run in your browser. This is normally the default condition for most browsers.
- If you are planning to help edit QUODLIBET, you will need to allow your browser to accept 'cookies.' This is normally the default condition for most browsers.

WELCOME

OK, now that we've set the ground rules, let's take QUODLIBET out for a test drive. Set your browser to the QUODLIBET web address (<http://www.datapunk.net/quodlibet/>) and before long you should be greeted with the following page:



The QUODLIBET main page

QUODLIBET runs under the DataPunk bioinformatics platform, so at the top upper right you will always see a navigation menu for other DataPunk functions. However we will always be in QUODLIBET so there is really no other reason (other than curiosity) to use these links.

The main panel is divided into two parts, on the left is a short description and news panel and on the right is a list of the available pathways, hereafter referred to as 'maps'. Each map has a short description and a link to its main canvas.



QUODLIBET main page link icons.

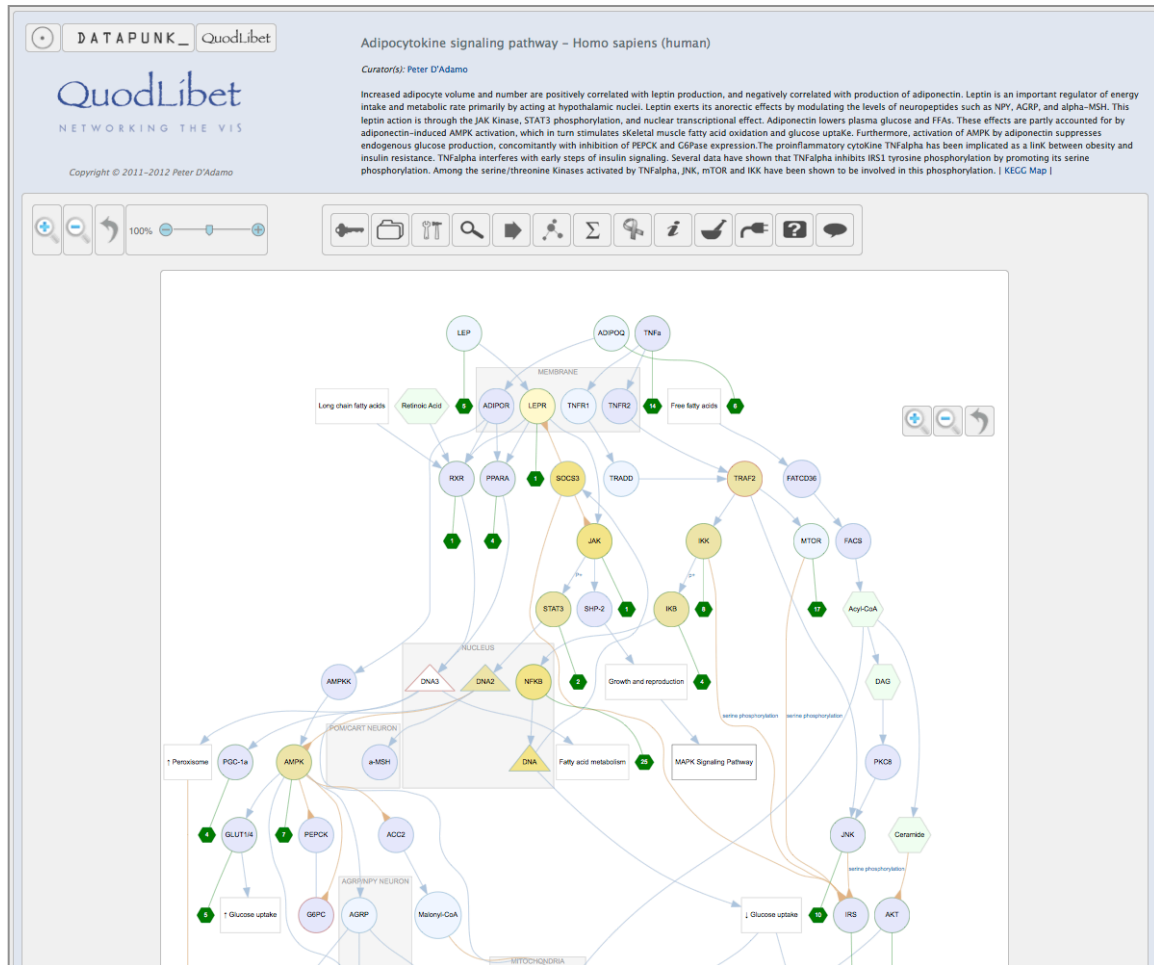
Above the list of the available pathways there are several icon links. They are:

- *Login (key icon)*: Clicking here allows you to log into QUODLIBET and editor map files. Once you know your way around, you can log in as a guest and experiment with drawing a network map in the Sandbox, a special canvas for newbies.
- *Read User Guide ('i' icon)*: Clicking here opens up the User Guide, the document you are now reading
- *Visit Forum ('talk balloon' icon)*: Clicking here takes you to the QUODLIBET Community Forums

However, we will go directly to a QUODLIBET network map and have a quick look around, so click the link to *The Notch Signaling Pathway*.

THE QUODLIBET MAP SCREEN

The Notch signaling pathway is a highly conserved cell signaling system present in most multicellular organisms. QUODLIBET lets you explore it in a number of ways. Let's take a look at the basic screen:

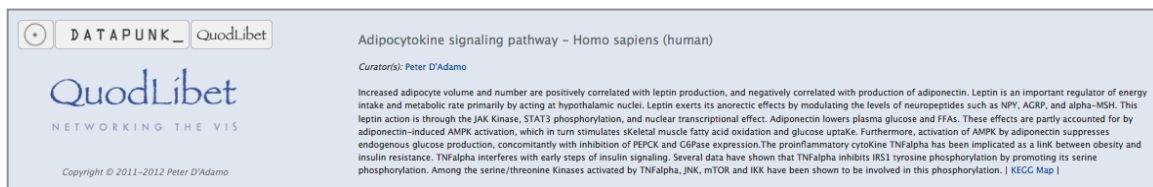


The Basic QUODLIBET network depiction screen.

The QUODLIBET screen is divided into a series of subsections. The following sections will discuss these in detail.

THE UPPER INFO AREA

The upper area of QUODLIBET contains several links. The circle with a dot inside icon links to the website of the UB Center of Excellence in Generative Medicine. The DataPunk Logo takes you back to the main DataPunk page. The upper area also shows the title and description of the map being displayed and the current curators of this map.

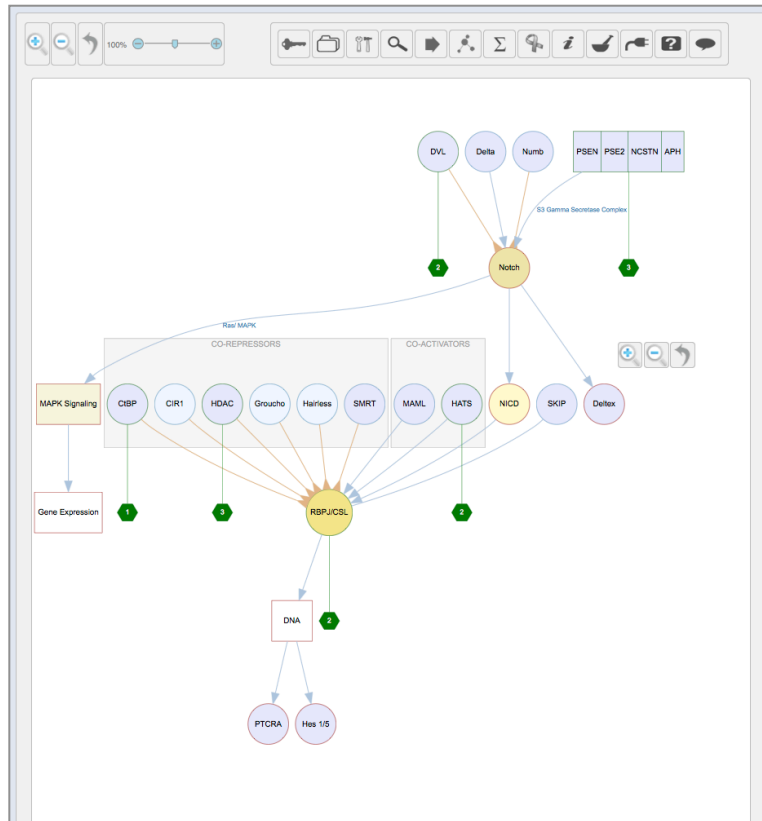


The screenshot shows the upper information area of a map in the QUODLIBET interface. On the left, there is a navigation bar with a circular icon containing a dot, followed by the text 'DATAPUNK_' and 'QuodLibet'. Below this is the 'QuodLibet' logo with the tagline 'NETWORKING THE VIS' and a copyright notice: 'Copyright © 2011-2012 Peter D'Adamo'. The main content area on the right displays the title 'Adipocytokine signaling pathway - Homo sapiens (human)' and the curator's name 'Curator(s): Peter D'Adamo'. A detailed description follows, explaining the biological significance of the pathway, mentioning leptin, adiponectin, AMPK, and TNFalpha, and their roles in energy intake, metabolism, and insulin signaling.

QUODLIBET upper info area.

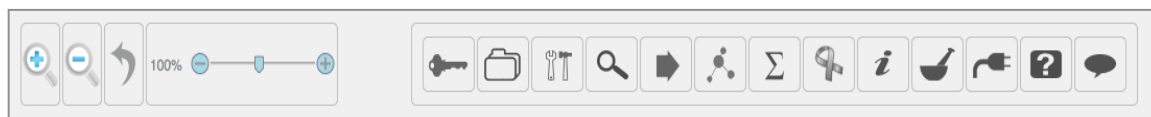
THE MAIN VIEWING AREA

The main viewing area of QUODLIBET contains several navigation controls and the main graph drawing area, the canvas.



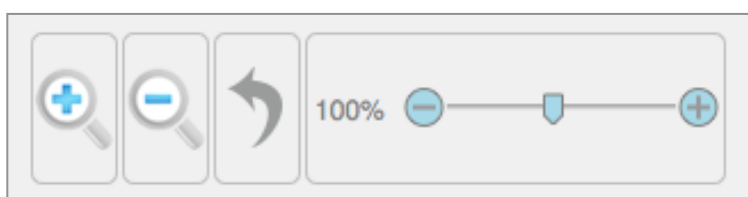
QUODLIBET main viewing area

NAVIGATION CONTROLS



QUODLIBET navigation controls.

The navigation controls allow you to control exactly how the graph will be displayed in the canvas and bring up a variety of special-purpose popup windows.



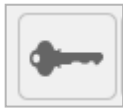
Map control menu

To the left are the controls that change the scale of the graph. Click on a magnifying glass icons link below to zoom in (+) or out (-). You can also use the mouse wheel to zoom. Click on the arrow icon to return to full size. You can control the exact percentage of zoom by adjusting the slide controls: left to zoom out the zoom, right to zoom in. When zoomed in, you can 'grab' the image in the canvas and move it around (pan it) by holding down mouse key and dragging it.

The other menu bar allows you to perform a range of special functions.



Special function menu



Log In Icon

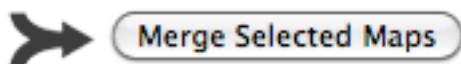
To the right you will see an icon of a key. Clicking this allows you to login (logging in allows the graph to be further edited.) Logging in is one of the ways that QUOLIBET generates a 'pop-up' screen so make sure that pop-ups are allowed by your browser, and that your desktop is not so cluttered as to obscure its appearance.



Map Browser Icon

Clicking this icon of a folder opens up a popup window that lists all the available metabolic maps. Clicking on any map will load it into the current canvas.

The map browser also allows you to select multiple maps that QUODLIBET will attempt to combine ('mash-up') into one large map. Up to three maps may be mashed together. To mash up multiple maps tick off the maps you wish to include and press the Merge Selected Maps button.

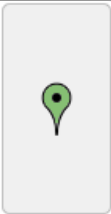


QUODLIBET will then do an internal check to see if the maps have connection points between themselves. If so, it will return a response listing the intersecting nodes and a map pin icon colored green. Click on the map pin icon to load a merged map into the main canvas. A map pin colored grey indicates that the maps do not share any intersecting nodes. Quodlibet will still offer to draw the map but they will not be connected in any computational way.

Intersection points shared by:

1. Apoptosis – Homo sapiens (human)
2. Autophagy – Homo sapiens (human)

- Apoptosis
- BCL2
- ER Stress





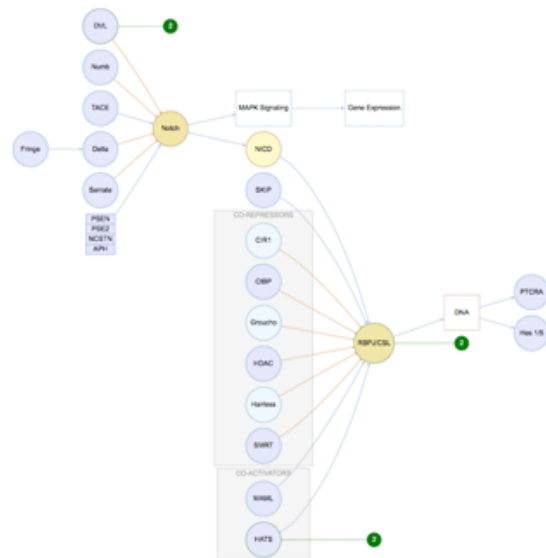
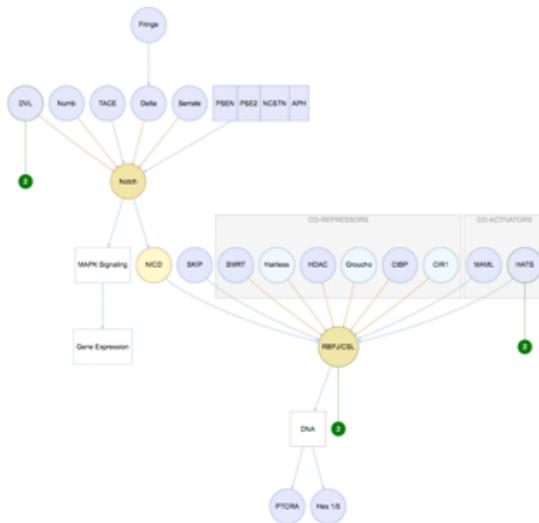
Search Maps Icon

This popup screen allows you to search for particular gene/protein/entities in the active canvas or across the entire network map library. You can search for up to three terms at the same time. When you click on any search result map, it will be loaded into the current canvas with the search node highlighted in red.



Map Orientation Icons

The arrow icon allows you to choose how QUOLIBET displays the graph: top-to-bottom (the default) or left-to-right.



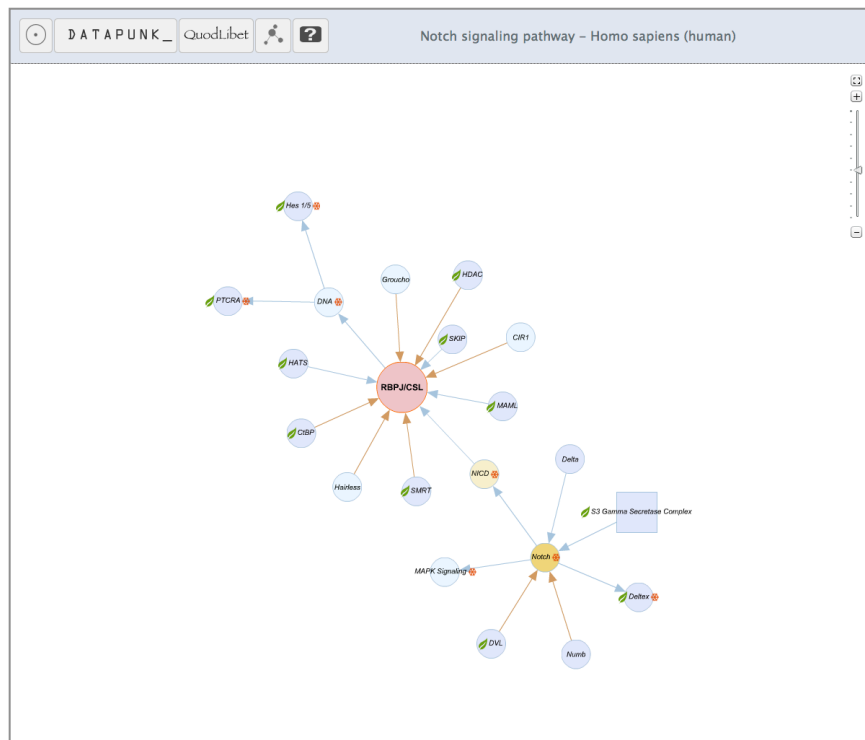
The two ways that a graph can be displayed in QUODLIBET.

Left: Ranking direction is from top to bottom. Right: Ranking direction is from left to right.



Constellation Roamer Icon

Constellation Roamer is another tool for visualizing QUODLIBET networks and their relationships. Clicking on this icon will open up a new main window tab in your browser. Unlike the Main Canvas, Constellation Roamer is designed to allow you to explore a network node by node. Choosing any node (by clicking on it) centers the graph on that node and then extends (radiates) the network out from that node by four degrees. In other words, clicking on any node will display the selected node, its neighbors, their neighbors, and their neighbors. Roaming a network is a different way of exploring relationships.



Constellation roamer window

The Constellation Roamer window has its own help popup, which can be accessed by clicking the link with the question mark icon at the top of the screen.



Analytics Icon

QUODLIBET does sophisticated network calculations that can be daunting to newcomers to graph theory. Using the Analytics (the 'sigma' character icon) pop-up opens up a pop-up window that is designed to provide a visual display of the performance of the network.

The Analytic pop-up features a 'heat-map' comprising a table organized by rows (the gene-protein nodes) and columns (graph functions). Each column is 'sortable' by clicking on the column heading; once to sort that low-to-high, then again to sort high-to-low.

Most columns are colored dark blue (high value) to white (low value). The second column (in-degree) is colored red-yellow-green because values veer from zero to either positive (more edges leaving the node than entering) or negative (more edges entering the node than leaving).

Clicking on the node name opens up the information panel for that node.

Quodlibet Analytics

You can click on a column heading to sort by that column. Click again to reverse the sort.

NAME	BETWEENNESS CENTRALITY	NODE IN-DEGREE	ADJACENCY MATRIX	NETWORK TOPOLOGY	PAGE-RANK	ASSOCIATED PROTEINS	ASSOCIATED AGENTS
CIR1	0	-1	3	23	5	0	0
CtBP	0	-1	9	11	14	56	0
DVL	0	-1	17	21	2	103	2
Delta	9	0	5	18	16	12	0
Deltex	0	1	4	8	20	30	0
Fringe	0	-1	16	19	3	6	0
Groucho	0	-1	15	17	8	0	0
HATS	0	-1	20	25	10	474	2
HDAC	0	-1	22	13	15	195	0
Hairless	0	-1	7	15	9	0	0
Hes 1/5	0	1	10	1	19	21	0
MAML	0	-1	24	24	13	17	0
NICD	32	0	11	7	21	0	0
Notch	56	3	19	9	24	84	0
Numb	0	-1	21	22	7	29	0
PTCRA	0	1	14	2	18	0	0
RBPJ/CSL	54	9	2	4	25	16	2
S3 Gamma Secretase Complex	0	-1	13	16	1	96	4
SKIP	0	-1	8	14	11	26	0
SMRT	0	-1	18	12	12	59	0
Serrate	0	-1	1	10	4	12	0
TACE	0	-1	12	20	6	12	5

QUODLIBET analytica pop-up menu.



Diseases Icon

Clicking the icon with the ribbon-like graphic opens up the diseases popup window. Here you can search for a particular disease and its representation in QUODLIBET. You can 'list all' diseases as well. Clicking on a disease link brings up the informational window for that disease, which includes a description, drug links, gene, biomarkers and other data. QUODLIBET uses the gene-linkage data about the disease to also list all metabolic maps that contain these linked genes and any naturopathic agents that have been associated with the genes or compounds.

QuodLibet
NETWORKING THE VIS

Refresh Window Go Back Close Window

Adrenal carcinoma

CANCER (ICD-10: C74)

Adrenocortical carcinoma (ACC) is a rare endocrine malignancy defined by a heterogeneous clinical presentation, dismal prognosis, and lack of effective therapeutic regimens. The incidence of ACC ranges from 0.5 to 2 cases per million people per year, accounting for 0.02% of all reported cancers. Unfortunately, most patients present with metastatic disease which reduces the 5 year survival rate to less than 10%. Oncogenes and tumor-suppressor genes involved in adrenal carcinomas include mutations in the p53 tumor-suppressor gene and rearrangements of the chromosomal locus 11p15.5 associated with IGF II hyperexpression. Deletions of the ACTH receptor gene have recently been found in undifferentiated adenomas and in aggressive ACCs.

Commentary:

- ICD-O: 8370/3, Tumor type: Adrenal cortical carcinoma

Drugs:

- Mitotane [Link 1](#)

Markers:

- KI
- 67

Quodlibet Map: Steroid biosynthesis – Homo sapiens (human)
Quodlibet Map: Pentose phosphate pathway – Homo sapiens (human)
Quodlibet Map: Insulin signaling pathway – Homo sapiens (human)
Quodlibet Map: Amino sugar and nucleotide sugar metabolism – Homo sapiens (human)
Quodlibet Map: Fructose and mannose metabolism – Homo sapiens (human)
Quodlibet Map: Apoptosis – Homo sapiens (human)

Typical disease informatics popup.



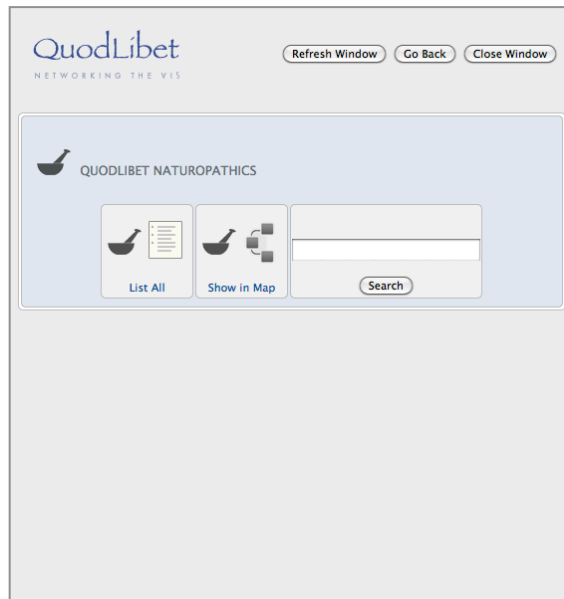
Information Icon

Clicking the icon opens up the current QUODLIBET User Guide pdf file.

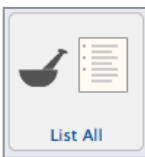


Naturopathics Icon

Clicking the icon with the mortar and pestle graphic opens up the naturopathics popup window. The popup displays as a sort of 'dashboard'



Naturopathic dashboard informatics popup.



Clicking on the 'List All' link will display a list of all naturopathic agents or procedures currently included in the database. Clicking on any of the listed agent will bring up the informatics screen for that agent.

Baicalin references used by Quodlibet:

1. [Baicalin, a flavone, induces the differentiation of cultured osteoblasts: an action via the Wnt/beta-catenin signaling pathway.](#)

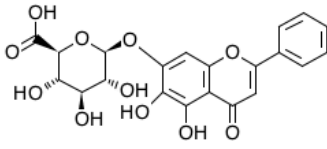
J Biol Chem 2011 Aug 12;286(32):27882-93

Search PubMed Thru Datapunk

Baicalin

All Results 20 Items per page Search Datapunk

KEGG

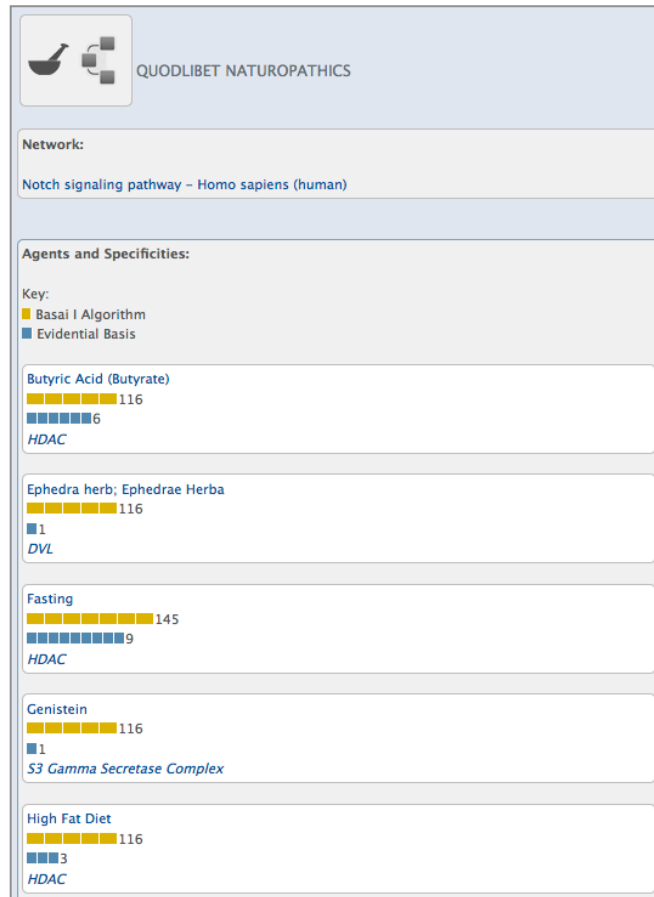
Entry	C10025	Compound
Name	Baicalin; Baicalein 7-O-glucuronide	
Formula	C ₂₁ H ₁₈ O ₁₁	
Exact mass	446.0849	
Mol weight	446.361	
Structure	 <p>C10025</p> <p>Mol file KCF file DB search Jmol KegDraw</p>	
Remark	BRITE hierarchy	

Naturopathic agent informatics popup.

Depending on availability, this screen may include information from a variety of external databases, including KEGG, PubMed, SWISSPROT, HPRD, etc.



Clicking on the 'Show in Map' link will open up a popup window that displays and analyzes all natural products included in the current active map.



Naturopathic agents in network popup.

This screen uses a unique algorithm (problem-solving formula) developed by Peter D'Adamo called the 'Basai I Algorithm.' It is a combination of different graph functions, matrices etc. that calculate the importance of where a naturopathic agent exerts its effects in a network, plus a coefficient determined by the evidential basis for its inclusion in the network. This algorithm generates a very sensitive result that can be used to add to any clinical decision-making approach.

Each agent that is linked to the active network is listed. The 'Basai Value' of the agent is depicted as a yellow power bar. The blue power bar is a crude estimate of the 'evidential basis' i.e. the quality of the evidence. Clicking on the name of the agent brings up the informatics screen for that agent. Underneath the blue power bar are listed the nodes whose regulation is associated with that agent. Clicking on these will bring up the informatics screen for that node.



Utilities Icon

Clicking on the icon that displays an AC power plug brings up the utilities popup. This screen contains a few helpful tools that allow you to search between different databases for unique IDs, such as the Enzyme Consortium (EC) number, the KEGG numbers, etc.



Help (Panic) Icon

Clicking on the icon that displays a Panic Button mark brings up the online help popup. This screen contains helpful information about getting up and going in QUODLIBET, including legend information about what the different colors and shapes signify.



Forums Icon

Clicking on the Go To Forums link (the 'speech balloon' icon) sends you to the QUODLIBET Forums. The Forums are organized into two basic categories, threads for users and threads for editors. Anyone can read the threads, but it is best to register (simple and secure) so that if you have any problems you can post about them and hopefully get help.

Forum

Forum	Topics	Posts	Last post
<input type="radio"/> Welcome to Quodlibet A quodlibet is a piece of music combining several different melodies, usually popular tunes, in counterpoint and often a light-hearted, humorous manner. The term is Latin, meaning "whatever" or literally, "what pleases."	0	0	No posts
<input type="radio"/> Quodlibet Users Forum Questions, tips and help to let you get the most out of Quodlibet.	2	2	Fri Dec 09, 2011 7:09 am Peter D'Adamo ↕
<input type="radio"/> Quodlibet Editors Forum Information, help and guidance so that you can help Quodlibet.	1	1	Fri Dec 09, 2011 7:27 am Peter D'Adamo ↕

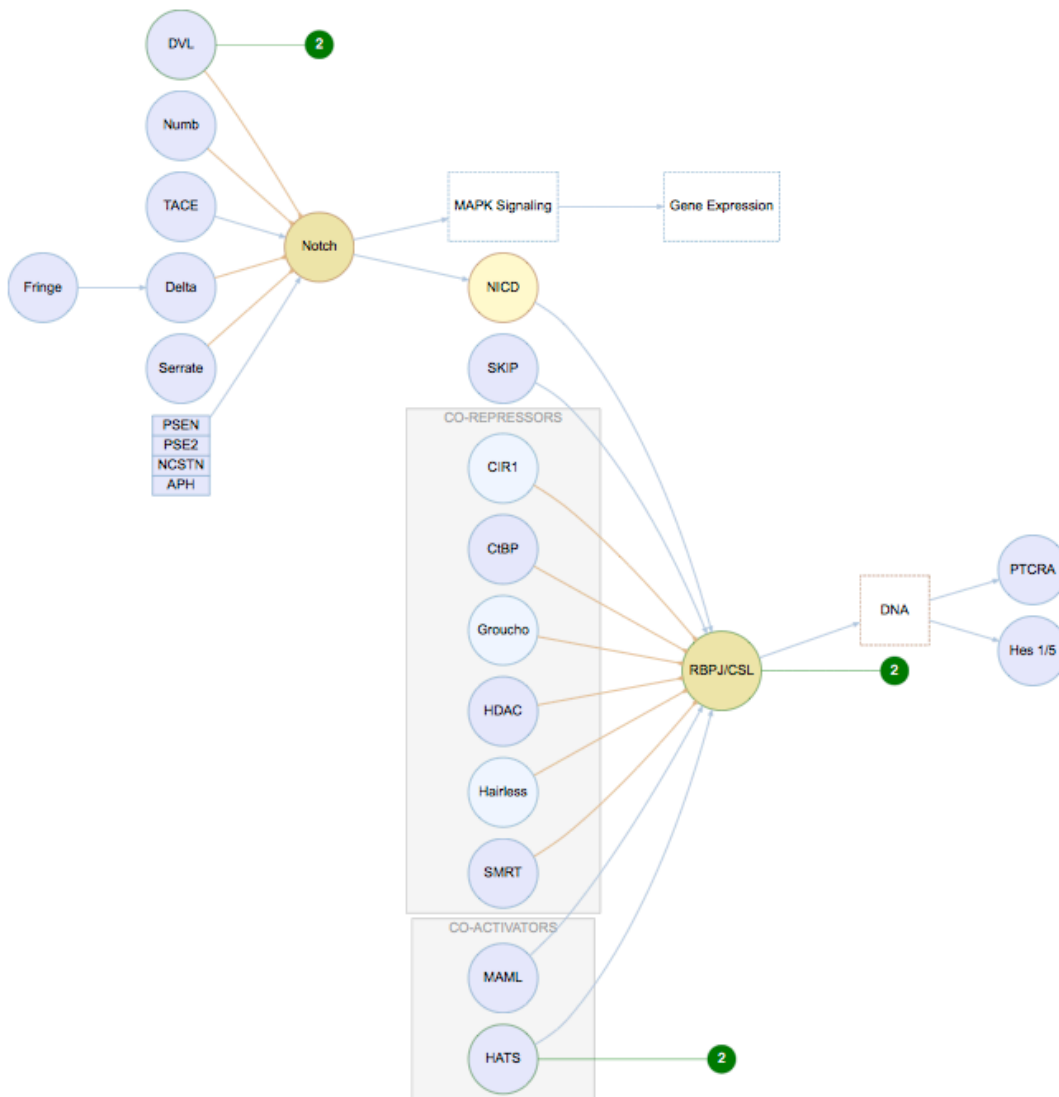
Quodlibet Map Projects

Forum	Topics	Posts	Last post
<input type="radio"/> MAPK Map Kinase Map A forum for discussing the MAPK Kinase map.	0	0	No posts
<input type="radio"/> Notch Signaling Pathway Map A forum for discussing the Notch Signaling Map.	0	0	No posts
<input type="radio"/> Sandbox Map A forum for discussing the Sandbox Map.	0	0	No posts
<input type="radio"/> New Map Suggestions What map should we do next? Your opinion matters.	0	0	No posts

QUODLIBET Forums

THE MAIN CANVAS

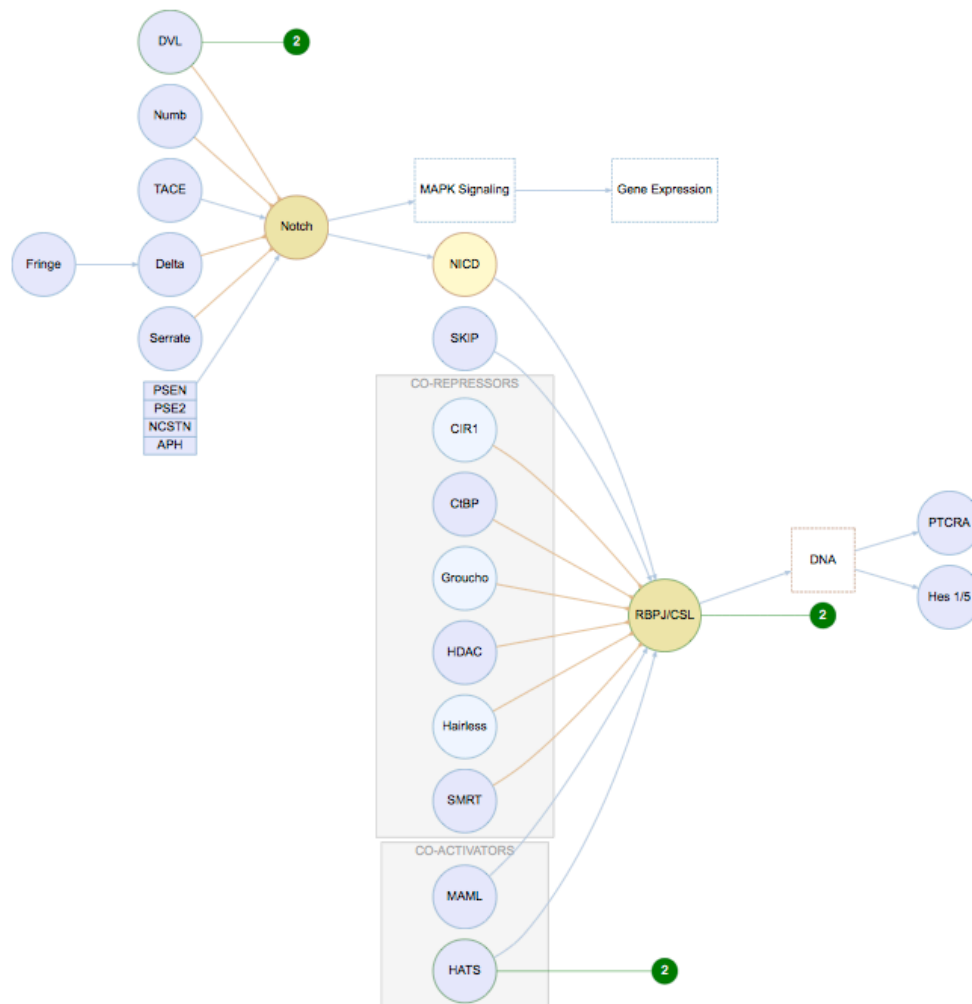
The main canvas is the heart of the information visualization system behind QUOLIBET. In order to best utilize QUOLIBET it is important that the user understand a few basics behind Graph Theory.



The QUODLIBET main canvas.

GETTING AROUND THE MAIN CANVAS

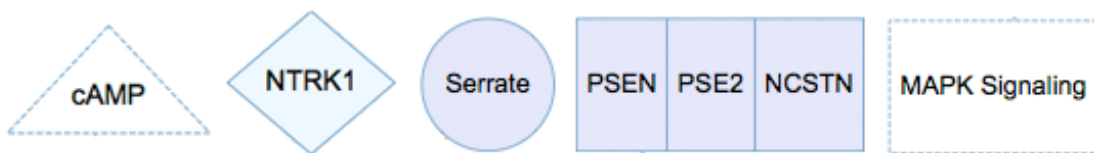
Now that we know a bit about graph theory, we can discuss just how network maps are depicted in QUODLIBET.



Notch network map in Left-Right display mode.

NODE SHAPES

Looking at the network we can see that the most common figures are circles. Circles are nodes and often represent genes or proteins. Another common node shape is the port, which is a rectangle comprised of two or more other named rectangles. By convention other shapes can include triangles, which often denote junction points; diamonds, which often denote receptor sites or other membrane entities, and uncolored boxes (often with dashed outline) that denotes a conceptual link or a link to another external process (such as a link to another network map).



Common node shapes (L-R): dashed triangle; diamond; circle node; port node; conceptual link.

EDGE SHAPES

Edge shapes are less varied, as only the arrowhead at the end of the edge has a shape. Edge arrowheads include the *standard arrowhead*, which usually means that the reaction/ activity is being promoted in that direction; and an *inverted or reverse arrowhead*, which signifies that the edge is providing some sort of inhibitory functions.



NODE COLORS

The characteristics of the node and its significance in the network determine node colors. Simple nodes (nodes that represent only themselves) are colored light blue. Complex nodes (nodes that represent collections of constituents) are colored lilac. Constituents in complex nodes represent elements that if depicted individually would simply clutter up the graph without providing any extra information.

For example:

The node labeled 'DVL' in the Notch map indicates the gene complex commonly referred to as 'Disheveled.' Disheveled has three particular variants: DVL1 (Disheveled I), DVL2 (Disheveled II) and DVL3 (Disheveled III). The information about each of these elements is 'contained' in the complex node DVL. Because DVL is a complex node it is colored lilac to alert you to that fact.

Other node colors can be generated dynamically by QUODLIBET. For example, highly 'connected' nodes are colored various shades of amber to denote their 'degree' of betweenness centrality. Nodes with a high page rank are denoted with a red border

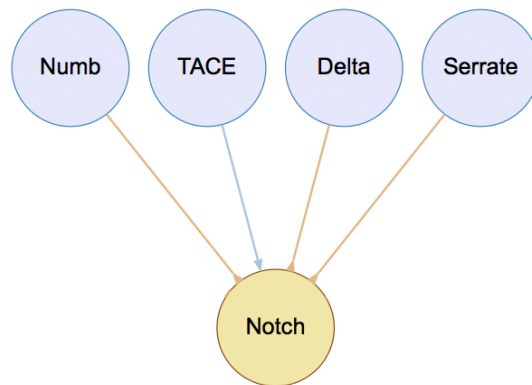


Node colors. CACN is a basic one-element node. SKIP is a complex node.

Notch and NICD are highly connected nodes; Notch has a higher betweenness centrality than NICD.

EDGE COLORS

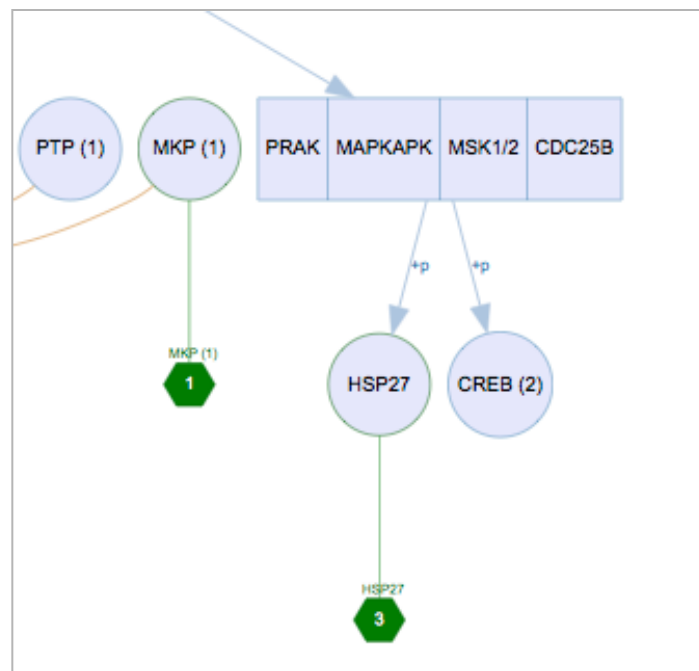
As with shape, edge colors are less complicated. Directed edges with normal arrowheads are dark blue colored. Edges with inverted arrowhead (inhibitory edges) are colored dark brown.



Edge colors. Numb, Delta and Serrate are inhibitory to Notch, whilst TACE has an activation effect.

SPECIAL NODES AND EDGES

Besides the typical node and edge decoration, several types of special nodes are possible in QUODLIBET. The most common is the *natural product flag (NP flag)*. This is a special tag that indicates that QUODLIBET has found referenced research studies reporting on a naturopathic agent or procedure shown to influence the function or expression of a gene or protein node. NP flags are small nodes colored dark green and an edge that extends to the indicated node. Nodes with NP flags have a green border around them and number in white that indicates the number of naturopathic agents currently known to be associated with that node. Clicking on the flag opens up a pop-up window giving details and the Pub Med abstract for the reference articles.



Nodes MKP and HSP showing a natural product flag (NP Flag) MKP has on agent associated with it, while HSP27 has three.



FLOATING BAR MENU

As you move the main canvas up or down you will see that a small 'floating menu' follows your movements. This small menu contains zooming controls similar to the main top toolbar. It also features three 'visibility controls' and a quick link to the Help popup.

Visibility Controls

Three buttons control whether certain features will be displayed on the main QUODLIBET canvas. These are:



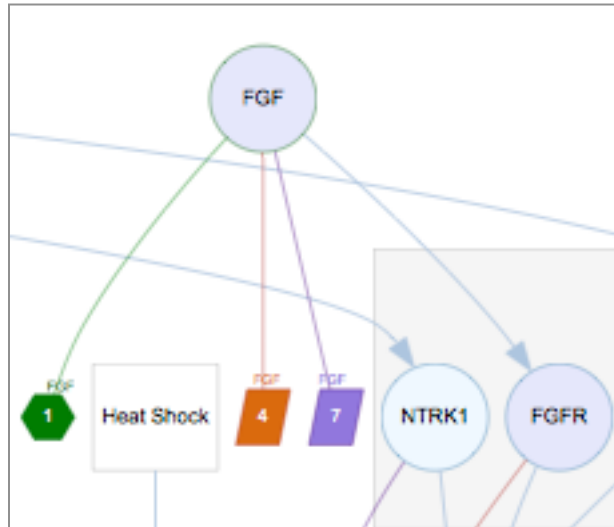
Turn naturopathic NP flag display on/off.

If you click on the hexagon icon in the floating menu it will show the naturopathic agent flags. By default this button is set to display naturopathic agents.



Turn SNP and CNV flags on/off.

If you click on the rhomboid icon in the floating menu it will show links to genes with either copy number variant (CNV) data and/or single nucleotide polymorphism (SNP) data. The CNV links are purple-colored rhomboids, the SNP links are orange-colored. Clicking on the CNV links brings up pubmed data on the CNV while clicking on the SNP link provides data on the most clinically significant SNPs linked to that gene and linkouts to NCBI refSNP, PubMed and SNPpedia if these sites feature entries. By default this button is off.



Nodes FGF showing a green natural product flag (NP Flag) indicating that one natural product is associated with this node. With the SNP/CNV button toggled on FGF also shows that four clinical significant polymorphisms (SNPs) are associated with this node and a total of 7 Pubmed article are associated with copy number variants (CNV) known to be linked to this gene.



Turn Network Motif highlighting on/off.

If you click on the network motif button in the floating menu it will redraw with map with Feed-Forward Loops (FFL) highlighted in red. By default this button is off.

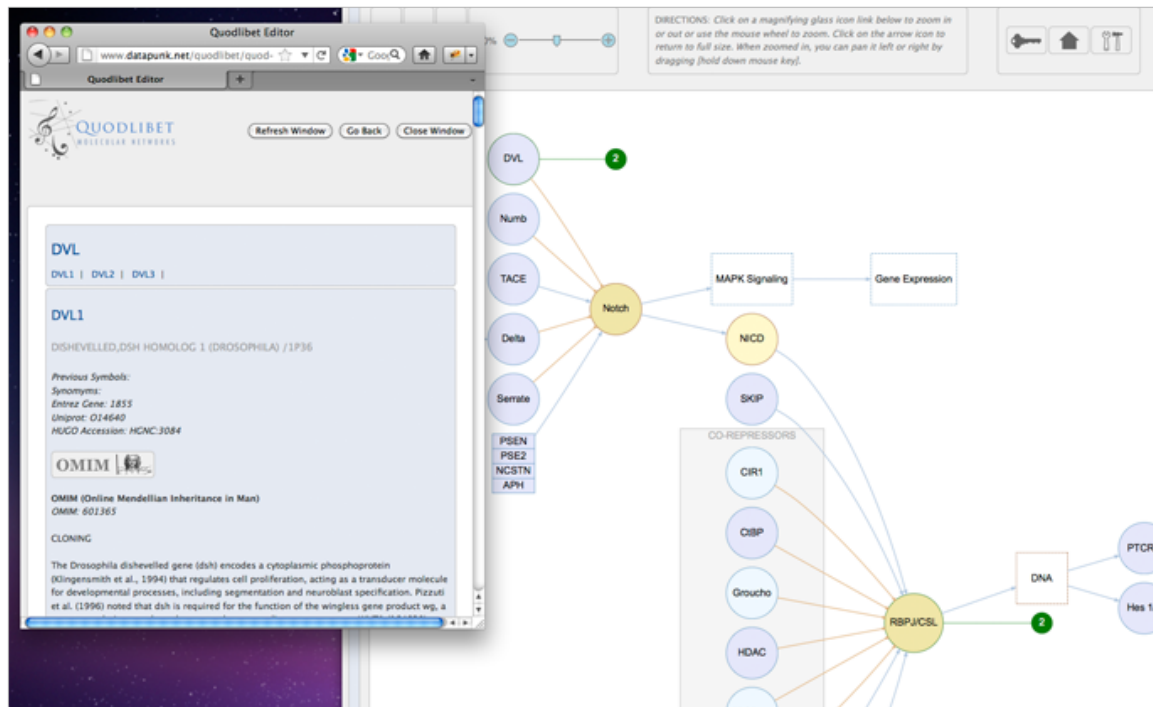


Open Help pop-up window.

If you click on the help (panic) button in the floating menu it will open up the Help Screen in the popup window.

POP-UPS AND HYPERLINKS

Clicking on any node, NP flag and many edges will activate a pop-up window that contains detailed information on that entity.



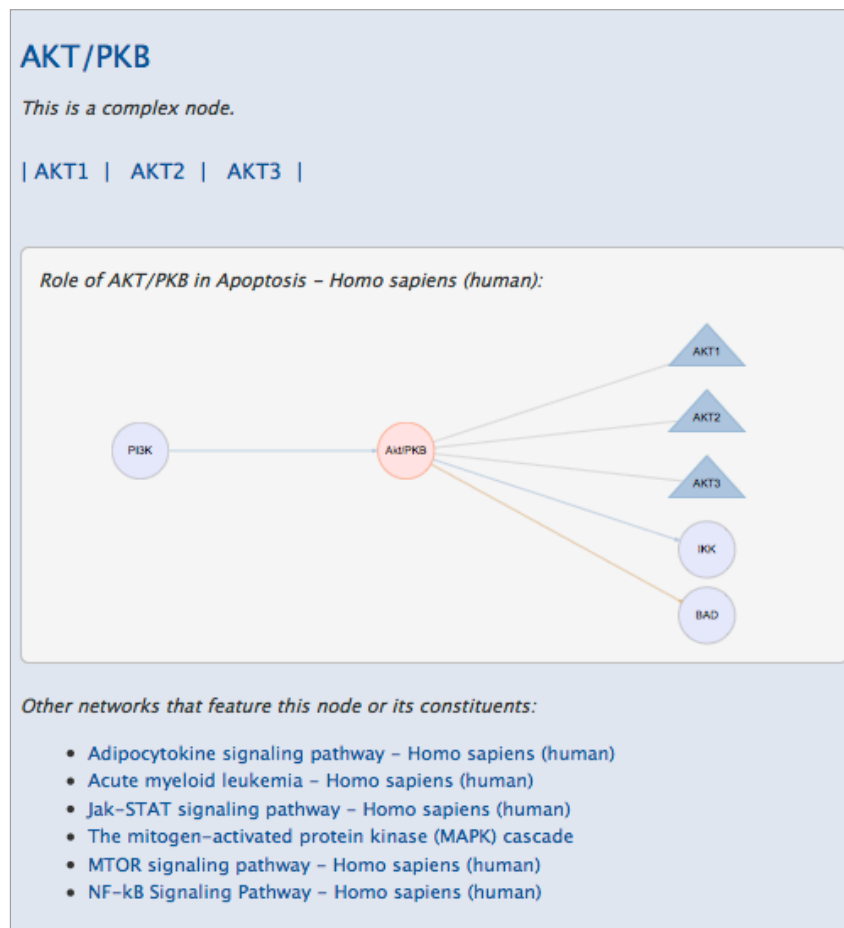
Clicking on node DVL opens up the pop-up display for that node.

When you click on a node, the pop-up will display information about that node (including information about the elements in that node if the node is complex.) This typically includes entries about the node from OMIM (Online Mendelian Inheritance in Man) and HPRD (Human Protein Resource Database).

When you click on a NP flag, information will be displayed listing the natural products linked to that node and the Pub Med abstract that supports it.

NODE DETAIL POPUP

Clicking on any node in the main canvas opens up the node detail popup window, which features a treasure-trove of information on that gene/protein node. Let's have a look. In this case we've clicked on the AKT/PKB node in the *Apoptosis* map:



Top view of the Node Detail Popup

From the top you will see the name of the node and a flag to tell you whether the node is complex. Complex nodes act as 'holders' for more than one gene or protein. In this case AKT/PKB is complex because it act as a holder for genes AKT1, AKT2 and AKT3.

Following that is a simple 'jump table' that takes you to the specific entry detail(s) for the node and any constituents it contains if it is complex.

Below that is a miniature network, similar to what is seen in the main canvas. The node that is being spotlighted in the popup is always in the center, in pink. Nodes in the network that link to the node being profiled are on the left; links that lead from the profiled node to other nodes in the network are on the right. You can click on any node in the window to have the popup window profile this node, *which is a great way to move around (cycle) a network, especially if it appears highly complex in the canvas*. Special nodes may show up that appear as blue triangles, these nodes contain information about Copy Number Variants (CNV) that are associated with the profiled node. Clicking on a CNV node usually brings up a PubMed reference with further information.

Below the graph is

- A list of any other networks that include the profiled node, if available
- A list of naturopathic agents known to be associated with the expression of the genes or proteins associated with this node, if available
- A list of any outside web links associated with this gene/protein entity, if available
- The OMIM (Online Mendellian Inheritance in Main) entry for is gene/protein entity, if available
- The HPDB (Human protein Database entries for any proteins associated with this gene/protein entity, if available

THE QUODLIBET COMMUNITY

We hope that this guide has peaked your curiosity about becoming a full-time QUODLIBET editor. Systems like QUODLIBET evolve into a community of knowledge workers intent on producing an exemplar of modern knowledge, a type of work that is best done singularly, but in a highly collaborative way.

THE FUTURE

As of this moment (December 2011) QUODLIBET is just coming out of development. Most of the initial programming is complete and a reliable means of information exchange has been created (Naturopathic Systems Biology Markup Language.)

I am working on increasing bench performance and reliability. There are only two maps currently available (Notch and Map Kinase Cascade) and both are incomplete. However, there is a fully functioning Map Editor that is also completely browser-based, intuitive, and fun to use. What is needed now is the community of volunteers who would be willing to devote time to curate additional maps. Hopefully this call to action will not prove too disappointing: I can think of no better way to enhance one's own understanding and knowledge about a complex topic than to build mind-maps. Thus it is to the students of our profession that I direct this challenge, though any interested party with a computer and a decent Internet connection is welcome to help out.

Phase I of our map development program will involve translating the KEGG genomic and metabolic maps into QUODLIBET format. KEGG maps are good and even hyperlink to relevant KEGG entries for enzyme activities, drugs, etc. However KEGG

maps are hand drawn and cannot perform network graph computations. However KEGG has done much of the heavy lifting: converting a KEGG map to a QUODLIBET map makes development quick and painless. From there QUODLIBET will link all subsequent maps into *clustered networks*, allowing for greater and greater information processing.

JOINING THE PROJECT

So I invite you to consider working in QUODLIBET. If you are the type of person attracted to this type of project, contact me at peter@dadamo.com and I'll send along the QUODLIBET Editors Guide. You will be up and running in no time. If you are interested in working on the further development of QUODLIBET and have good experience in Perl programming and Javascript, feel free to contact me as well.

I'd like to thank Martha D'Adamo, who was so very supportive of this project; Mitch Bebel Stargrove, who keeps me thinking about the Vis; Bob Messineo, who keeps a watchful eye on things; my students at the University of Bridgeport College of Naturopathic Medicine, and the entire Perl programming community (in particular CPAN, the Comprehensive Perl Archive Network) who have produced many of the helpful modules that I was able to incorporate into QUODLIBET and thus avoid the need to re-invent the wheel.

See you on the Forums.

Peter D'Adamo, ND

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