

PathBubbles

Version 1.0

Manual

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November 16, 2014

Introduction

PathBubbles is a web-based application of biological pathway visualization and analysis, allowing users to visualize, search pathways from Reactome, to upload their own gene data for ortholog analysis, and to upload their gene expression data for expression analysis. This is a web-version of PathBubbles project: <https://sites.google.com/a/umbc.edu/pathbubbles/> .

The current version is "1.0".

It is freely available at <http://raven.anr.udel.edu/~sunliang/PathBubbles/> (see Figure 1).

All the code is hosted on Github, you can fork it through the link: <https://github.com/yongnanzhu/PathBubbles> .

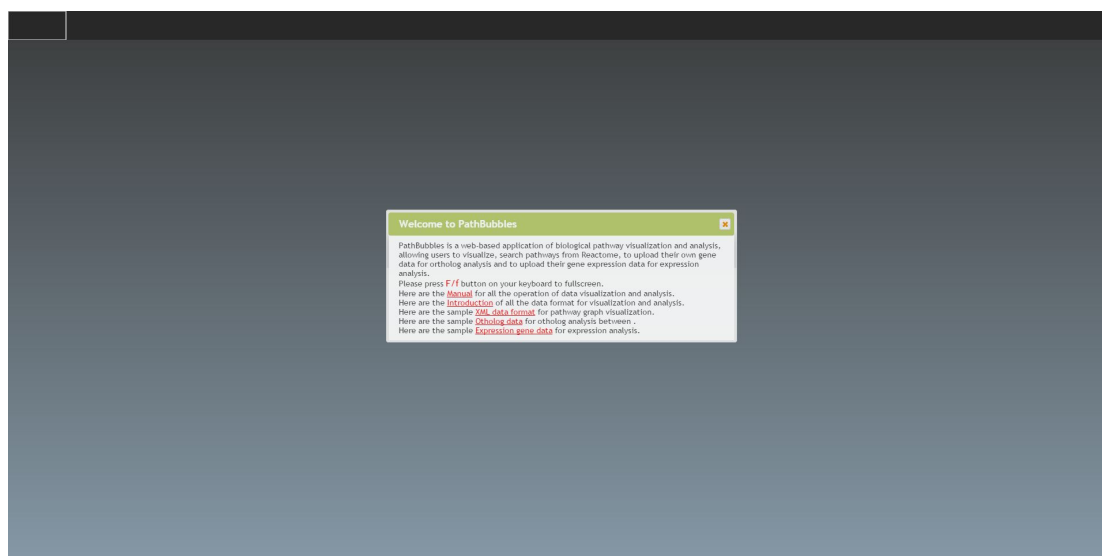


Figure 1 homepage of PathBubbles

Browser requirements

All modern ones, such as Safari, google chrome (best), and IE are supported. Please do not use FireFox. You can visit [Google support](#) for more information.

Supporting Pathway network format

The pathway graph in Pathbubbles supports pre-defined XML format. We will first show you the sample example, and then tell you the detail format.

```
<?xml version="1.0" encoding="utf-8"?>
<Pathway>
  <compartmentBlock Num="3">
```

<https://github.com/yongnanzhu/PathBubbles>

```

    <compartment j="0">
      <Name>early endosome membrane</Name>
    <Position>(0.40767891088437735,0.2510594446429637,0.18464217823124535,0.2294125895309596
4)</Position>
    <Contain>(C,1,,S,1,,S,14,,S,4,,S,6,,S,8,,S,9,,S,15,,S,16,,S,19,,S,20,,S,24,,S,26,,S,29,,S,30,,S,34,,
S,36,,R,1,,R,2,,R,3,,R,4,,R,5,,R,6,,R,7,,)</Contain>
    </compartment>
  </compartmentBlock>
  <complexBlock Num="7">
    <complex j="1">
      <Name>PIKFYVEVAC14FIG4</Name>
    <Position>(0.6283649298613249,0.5706117201901926,0.042311567567274076,0.027386127875
258303)</Position>
    </complex>
  </complexBlock>
  <physicalEntityBlock Num="1"/>
  <proteinBlock Num="15" />
  <DnaBlock Num="1"/>
  <RnaBlock Num="1"/>
  <smallMoleculeBlock Num="37"/>
  <reactionBlock Num="9">
    <reaction j="1">
      <Name>PI(34)P2 is dephosphorylated to PI3P by INPP4AB at the early endosome
membrane</Name>
      <Type>T</Type>

      <Position>(0.41048415733565263,0.2221266133316178,0.016924627026909632,0.0273861278
75258303)</Position>
    </reaction>
  </reactionBlock >
  <edgeBlock Num="41">
    <edge j="0">
      <Name>A</Name>
      <Ends>(P, 1, R, 1)</Ends>
    </edge>
    <edge j="39">
      <Name>J</Name>
      <Ends>(R, 8, S, 36)</Ends>
    </edge>
  </edgeBlock>
</Pathway>

```

The first line is about the standard xml tag. The formal pathway is a hierarchical structure.

The first type is compartment. Compartment has attributes with “Name” ,” Position” ,” Contain” . The position is a string with the combine of “x” , “y” , “w” , “h” of this compartment. For the “Contain” ,it is consisted of all the biomolecules of the compartment. Which is splited by “;” . For each biomolecule, it begins with its type, and id. The id is the index of this type.

In PathBubble, it has 6 types.

“C” for complex;

“P” for protein;
 “D” for Dna;
 “Rna” for Rna;
 “E” for “PhysicalEntity” ;
 “S” for small molecule;
 “R” for reaction

For each biomolecule, it has its id for “j” attribute.
 Its “Name” , its “Type”

At the end of the file is about the edges, which tells you the “Name” of the edge and Its two endpoints.

The endpoints is begins with the type of Biomolecule and the id of biomolecule, and ends with the type of Biomolecule and the id of biomolecule.

Supporting Pathway ortholog gene data format

You can upload you own gene data for ortholog analysis in PathBubbles.
 Below we will you show the gene data format, which is tab-delimited format.
 The first column is about the symbol of gene, and the second column is about the database Id of this gene.

symbol	dbId
ADA	\N
CDH2	414745
AKT3	421497
MED6	426282
NR2E3	395289

Supporting Pathway gene expression data format

You can upload you own gene expression data for expression analysis in PathBubbles.

Below we will show you the gene data format, which is tab-delimited format.
 The first column is about the gene id, the second column is about the symbol of the gene, and the third column is about the log based ratio of this gene in the expression experiment.

gene_id	symbol	ratio
374096	SMAD6	0.6892992938620315
395132	SMAD3	7.128911138923654
395247	SMAD2	3.370212765957447
395543	SMAD9	Infinity
395679	SMAD5	3.013579576317219
395680	SMAD4	2.3619197482297403
429683	SMAD7	0.647887323943662
374094	TGFBR1	6.733865119651922
396399	TGFBR2	0.45263157894736844
395934	SHC1	1.4310163243812535
426482	SHC4	Infinity
431265	SHC3	NaN
770341	SHC2	3.3697916666666665
386572	GRB2	10.56062819576333
423572	SOS2	1.4514200298953663
425964	SOS1	1.5194805194805194

Introduction of PathBubbles Interface

1. Full screen

You can press “F/f” on your keyboard to change to “full screen” Mode. If it is on the “full screen” Mode, you can press “Esc” on your keyboard to exit the “full screen” Mode.

2. Menu of the scene

In PathBubbles, If you right click on the scene, it will pop out a menu. (see Figure 2).

You can view individual pathway network graph by select “Open Pathway Graph” menu, It will add a Graph Bubble on the scene. You can view all the pathways in a tree-ring by select “Open Pathway TreeRing” menu, It will add a TreeRing Bubble on the scene. You can view the simple tutorial by select “Open Simple Tutorial” and you can delete all the bubbles on the scene by select “Delete All” .

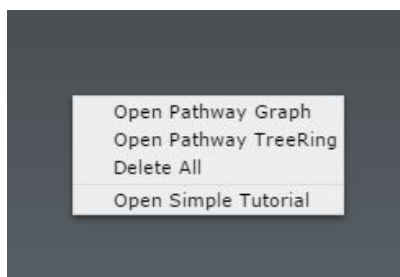


Figure 2

3. Menu of the Bubble

In PathBubble, all the bubbles can be group and ungrouped, and also they can be deleted. Every Bubble has a menu on the right corner (Figure 3 A, B, C) with three button (U/G, X, M). For the “U” button, this means the current bubble can be group (if it is overlap another bubble, they can be grouped), and if the “U” button become “G” , it means this bubble can not be grouped (if it is overlap another bubble, they can be grouped). “X” means close the bubble, you can delete the bubble from the scene just by clicking “X” button.

“M” mean functional menu for this bubble.(just Graph Bubble and Tree Ring Bubble has menu).

There are three types of bubbles could be added on the scene: Pathway Graph Bubble (Figure 3 A), Pathway TreeRing Bubble (Figure 3 B), Table Bubble (Figure 3 C). You can open Pathway Graph Bubble (Figure 3 A) and Pathway TreeRing Bubble (Figure 3 B) by selecting the context menu on the scene. Table Bubble (Figure 3 C) is selected from Pathway TreeRing Bubble. (Detailed description will be introduced in sections below).

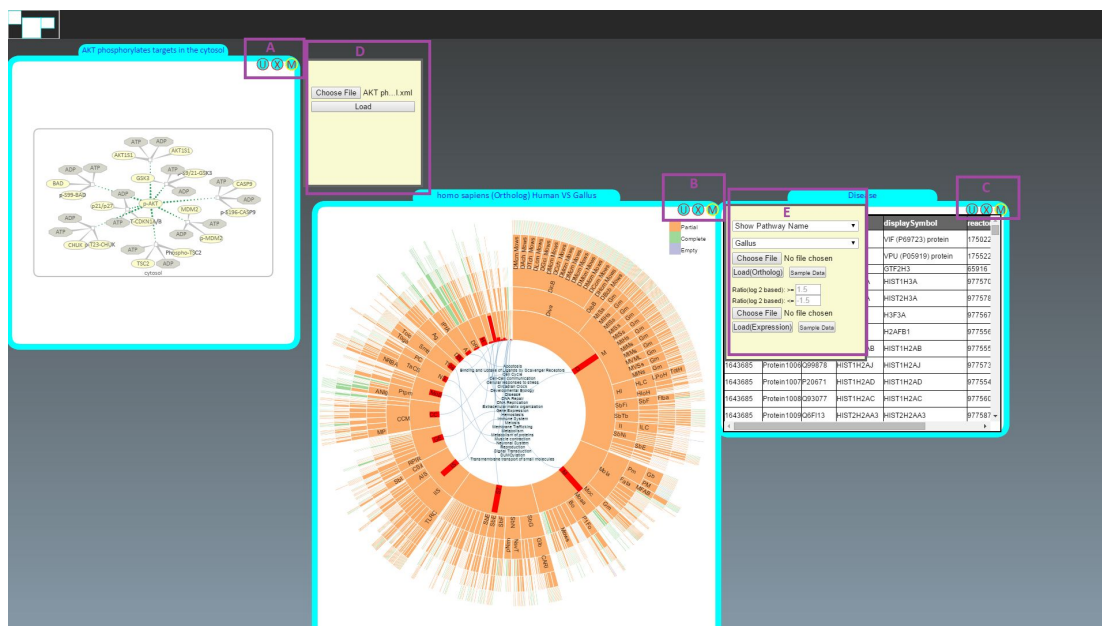


Figure 3

(1) Pathway Graph Bubble

You can view an individual pathway network graph by select “Open Pathway Graph” menu.

It will show you the default empty Bubble view (see Figure 4 A). And then you can click “M” button to open the functional menu on the right corner of the Bubble, you can choose the pathway network data to view the individual network graph (see Figure 4 B).

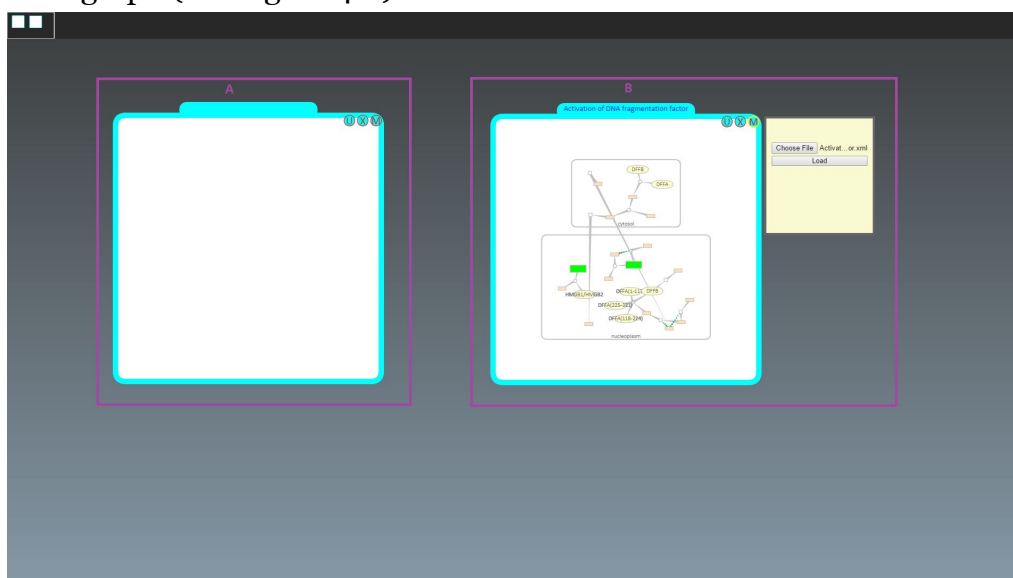


Figure 4

(2) Pathway Tree Ring Bubble

You can view all the pathways (1417 from Reactome) in a tree-ring by select “Open Pathway TreeRing” menu.
It will show you the default view. (see Figure 5)

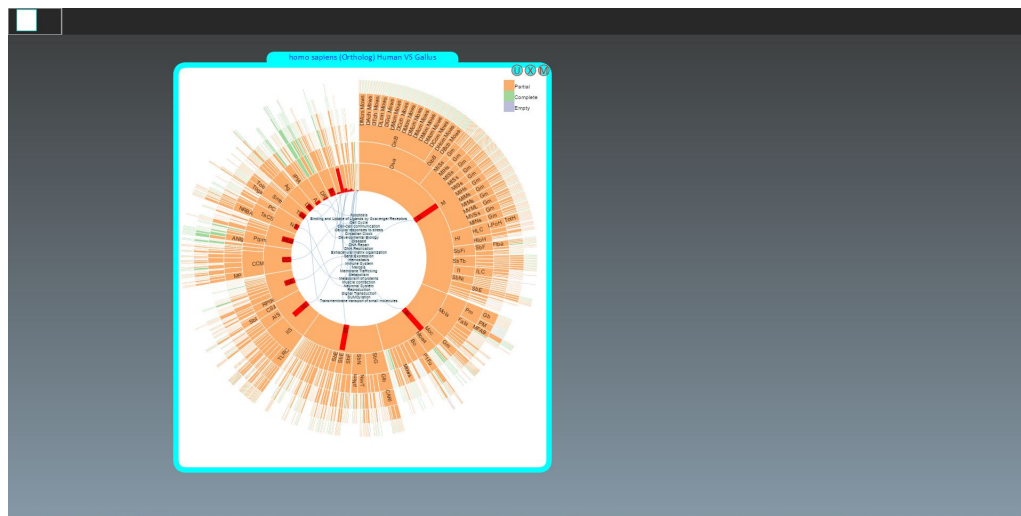


Figure 5

(3) Pathway Table Bubble

You can view the detailed protein information by “right click the bar (Figure 6 A)” or “right click the arc of each pathway (Figure 6 B)” on the TreeRing Bubble View. It will add a bubble (Figure 6 C) for (Figure 6 A), It will add another bubble (Figure 6 D) for (Figure 6 B).

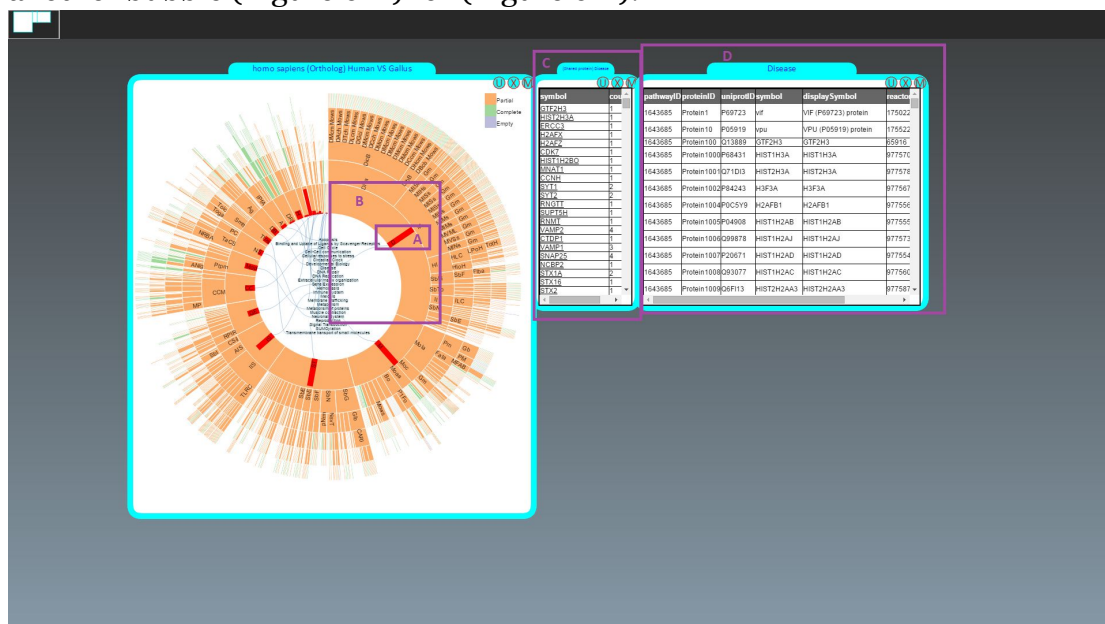


Figure 6

Introduction of PathBubbles Data Analysis

PathBubbles integrates all the existing pathways of Reactome (1417) in a single Sunburst (see Figure 5), and uses color to map interesting information, which is convenient to compare, query and validate hypothesis.

In PathBubbles, you can view each biological pathway network in a single Bubble (see Figure 4). You can find cross-talking relationship between different pathways, you can compare the ortholog information between different species. You can upload your own experimental data (gene expression data) to compare the result between different pathways, and figure out the detailed connect protein information by the Table view.

(1) Cross-talking Information

When you open a TreeRing, it will show you all the pathway names of the First Level of the TreeRing in the center. If you want to see the cross-talking relationship between pathways. You should click the “M” on the Menu Bar. And then, you should select “Show CrossTalk” option instead of the default “Show Pathway Name” option in the first dropDown menu. (see Figure 7) The crossTalking information showed in the graph represents the relationship between pathway in a same level. You can change the cross talking level by select the “crossTalkLevel” dropdown menu. (see Figure 7 B)

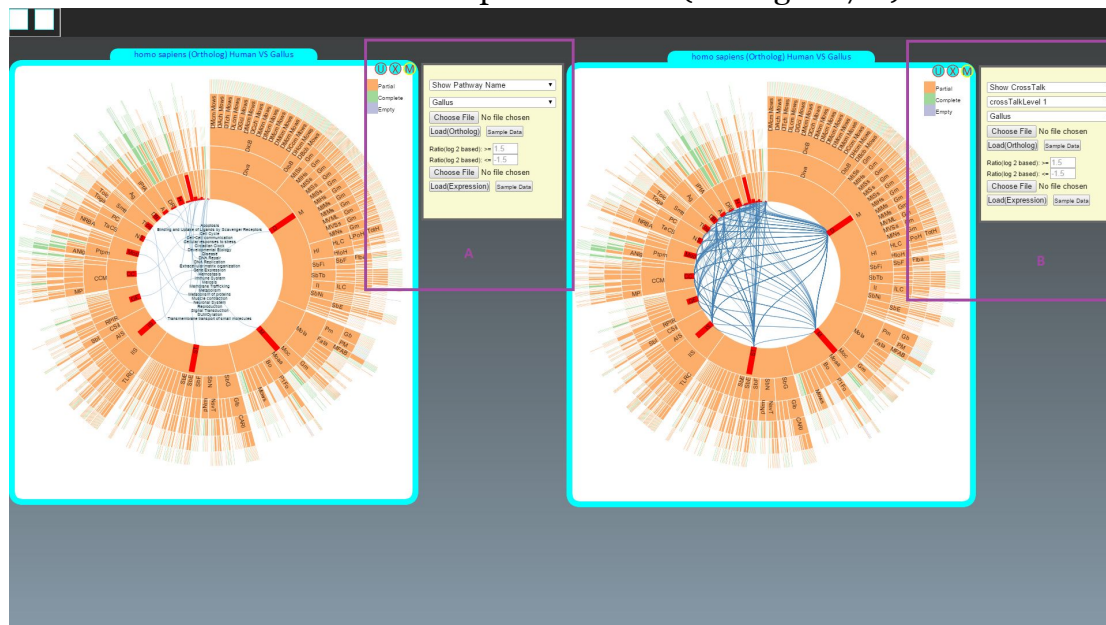


Figure 7.

(2) Ortholog Analysis

Our pathway is from Reactome, which is a database about human pathway. We can use the pathways of human to predict all the pathways' information

of other species by providing their gene information, so that we can know the pathway relationship between species. There are three types relationship between a species and human, Complete, Partial, Empty.

Complete: If all the gene of a species can be found in a pathway of human, we call this pathway is “Complete” to a species.

Partial: If just some gene of a species can be found in a pathway of human, we call this pathway is “Partial” to a species.

Empty: If all the gene of a species can not be found in a pathway of human, we call this pathway is “Empty” to a species.

In the PathBubble, all the three relationship of a pathway is encoded by color.” Yellow” for “Partial” ,” Green” for” Complete” , and “Purple” for “Empty” .

In the PathBubble, when you open a TreeRing, the default view will show you the ortholog relationship between Gallus and Human (see Figure 8 A). In the right corner of the Bubble, it will show you the color scale bar with 3 types of ortholog relationship (see Figure 8 B). And also you can view cross-talking information relationship by change “Show Pathway Name” (see Figure 8 C). You can change the default species by select “Choose Species” menu (see the right Bubble of Figure 8, which is selected “Alligator” option). You can upload your own gene data of a species by select your own gene file and load it. (see Figure 8 E).

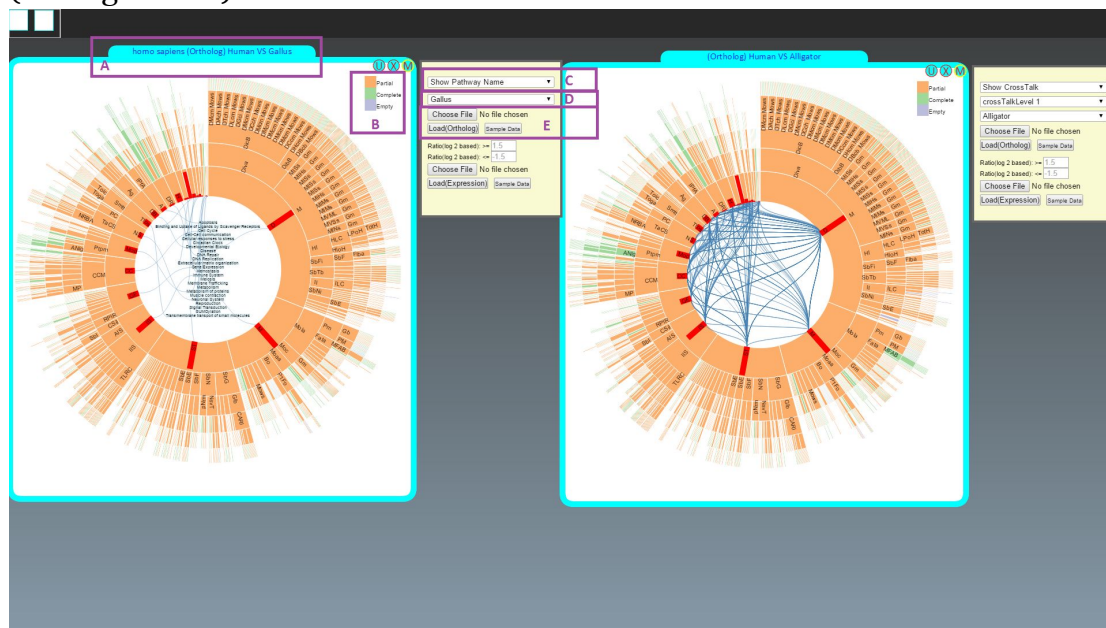


Figure 8

If you want to see the detailed shared protein information of a pathway between two species. You can right click a red bar on the ring. (see Figure 9 A) It will give a Table Bubble, which shows you the shared protein information of disease pathway between Human and Gallus. (see Figure 9 B) The Table is sortable, you can click the header of the table to sort it. And also If you care about the detailed symbol protein information, you can right click the

interested symbol name. (see Figure 9 C)

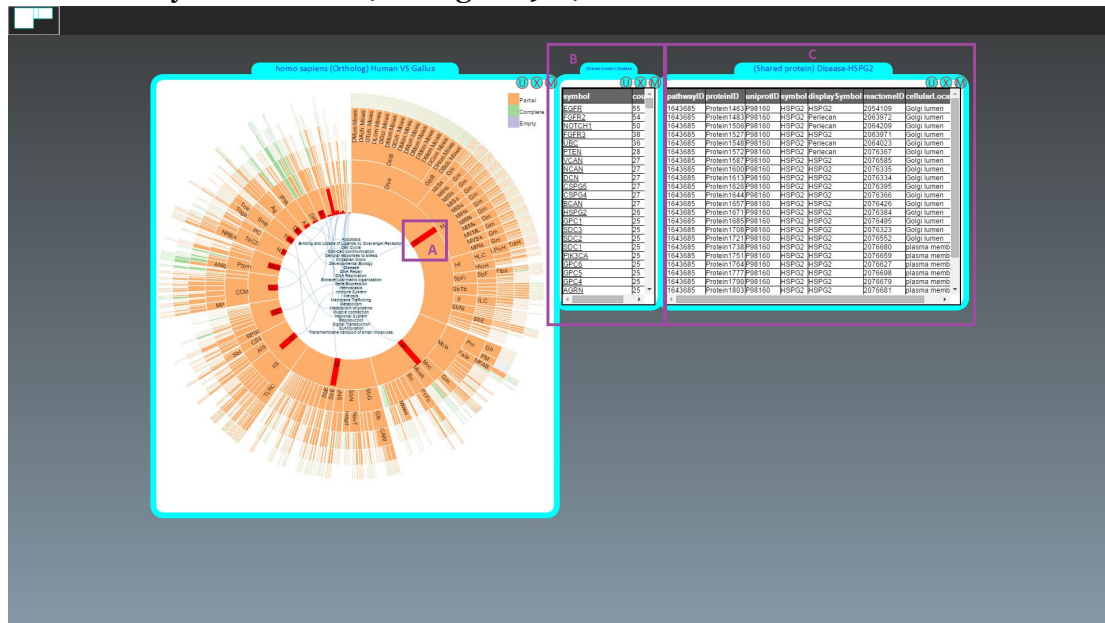


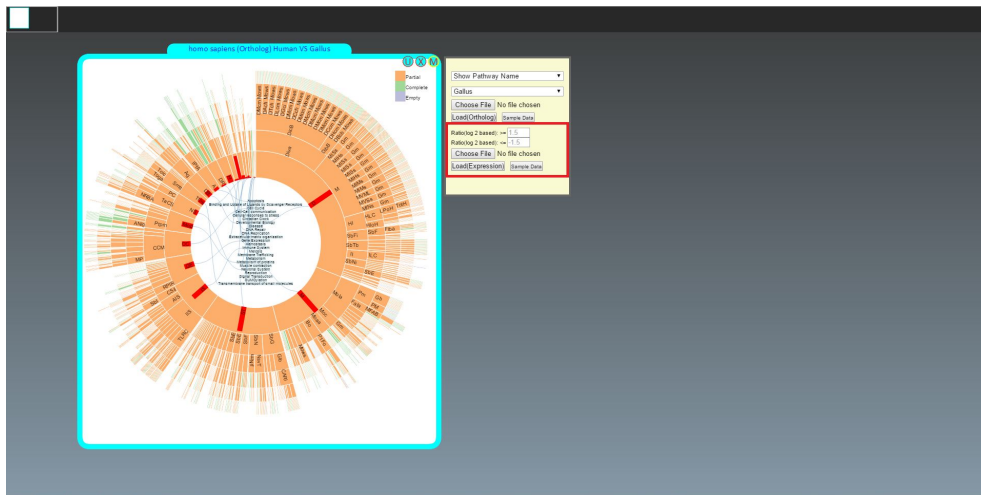
Figure 9

(3) Gene Expression Analysis

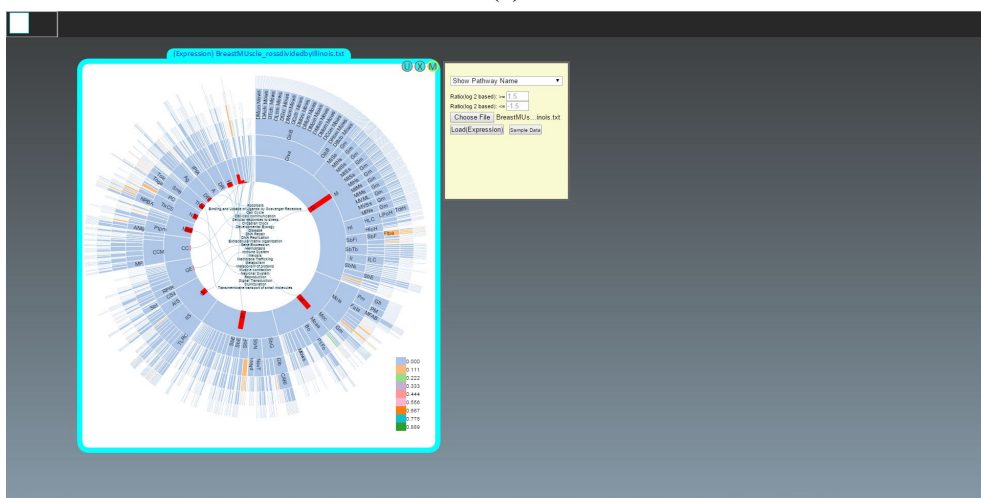
PathBubbles provide gene expression analysis for a certain species. Gene Expression analysis is based on a certain species. So at first, you need to do the “Ortholog Analysis” (see the previous section).

And then you can unupload your own gene expression data (see the expression data format section).

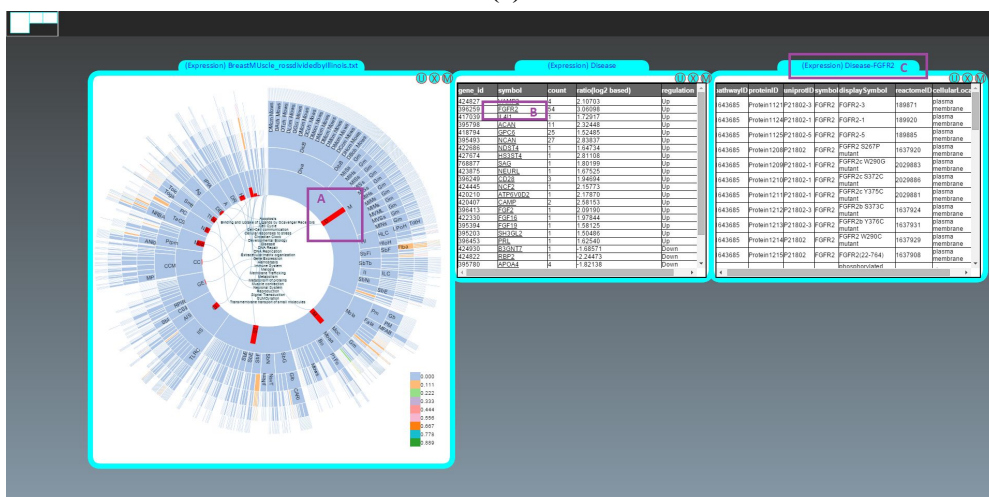
PathBubbles



(1)



(2)



(3)

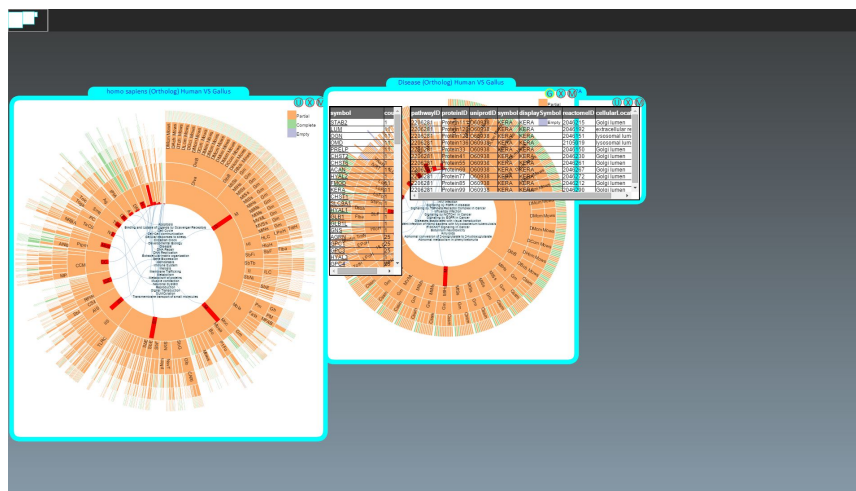
Figure 10

Introduction of PathBubbles Interaction

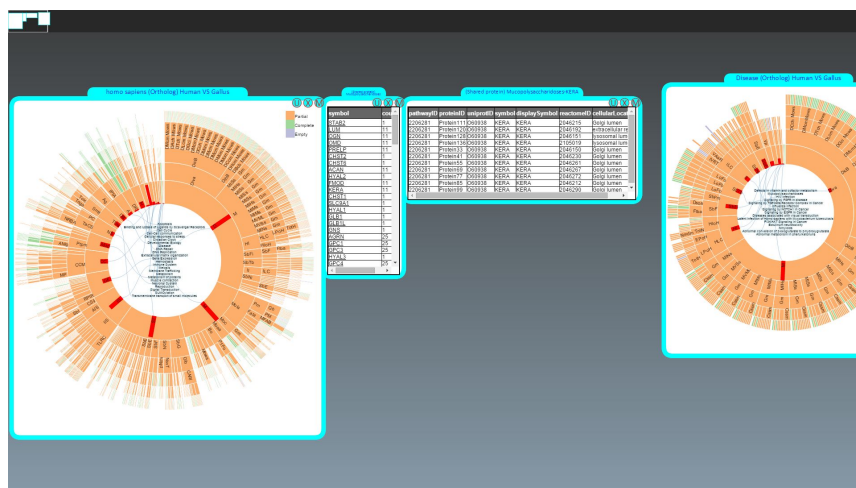
For the design of interaction. PathBubbles applies the idea of VisBubbles and CodeBubbles by extending static multiple views to a metaphorical interface of Bubbles, each of which is treated as a functional unit view. Bubbles do not overlap, they can be grouped and ungrouped. In PathBubble, You can select a bubble by mouse click the border of the Bubble or click its title. You can move it after you select it. If the selected bubble moved overlapped another bubble when you stop, they can be grouped if the “U” flag is on. (Figure 11 (1)) And If you want to ungroup a bubble from a group, you just need to click “U” button, after that, the label of “U” button will become “G” (Figure 11 (2)). And this bubble can be pop out, and also it can not be grouped, you can move it away.(Figure 11 (3))



(1) Group



(2) Click “U” of TreeRing in the Middle



(3) Move the ungroup bubble away
Figure 11

PathBubbles also applies the idea of “virtual desktop” by providing a navigation bar on the top and extending the current view space to much larger space. You can switch the view just by selecting the current viewpoint and

move it on the navigation bar. (see Figure 12)

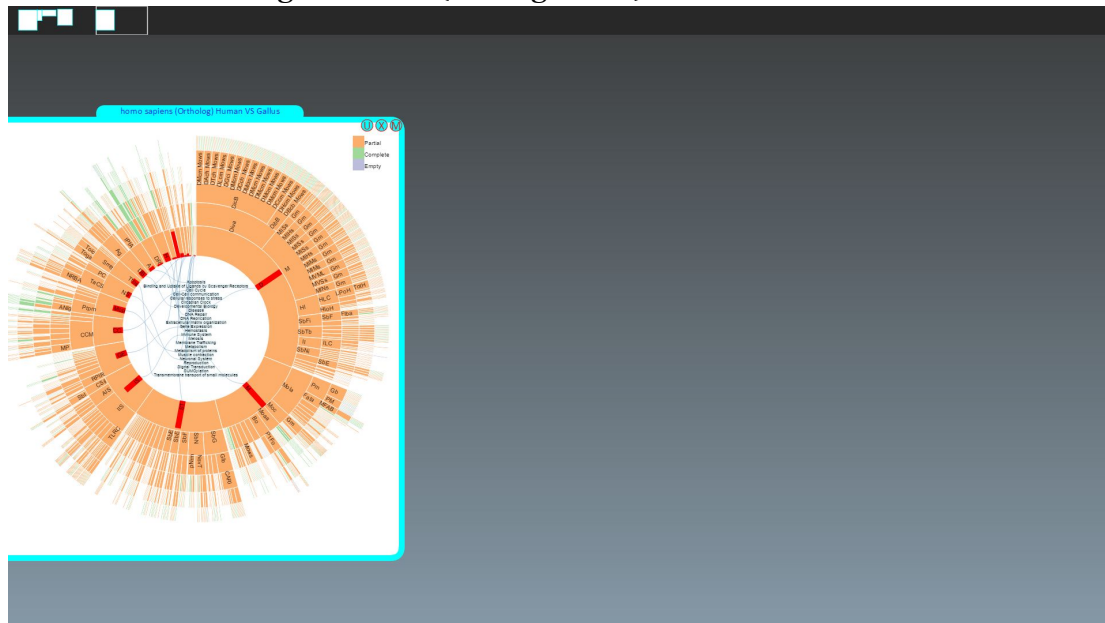


Figure 12 move viewpoint