

CCCExplorer

v1.1.0

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1. Installing CCCExplorer on Windows

Install JRE

CCCExplorer is a java based application. So the user needs to install JRE before using it.

The user can download JRE package from the link below.

<http://www.oracle.com/technetwork/java/javase/downloads/jre7-downloads-1880261.html>

Install R language and dependent packages

Download R language for Windows from <http://cran.rstudio.com/>

<https://cran.r-project.org/bin/windows/base/>

Install R 3.2-0 or upper version

Open RGui to install following packages.

```
>install.packages("igraph")
```

Run CCCExplorer

Decompress CCCExplorer_v1.1.0.zip

1. Double click “run.bat” to run it.
If you are using Linux or MacOS, run “./run.sh” command in your Terminal.
2. Click “setting” icon, there is a popup dialog. Click “Browse” button to find the Rscript.exe file.
3. After setting the path of Rscript.exe, you can select the files of source and target cell expressions to run your project.

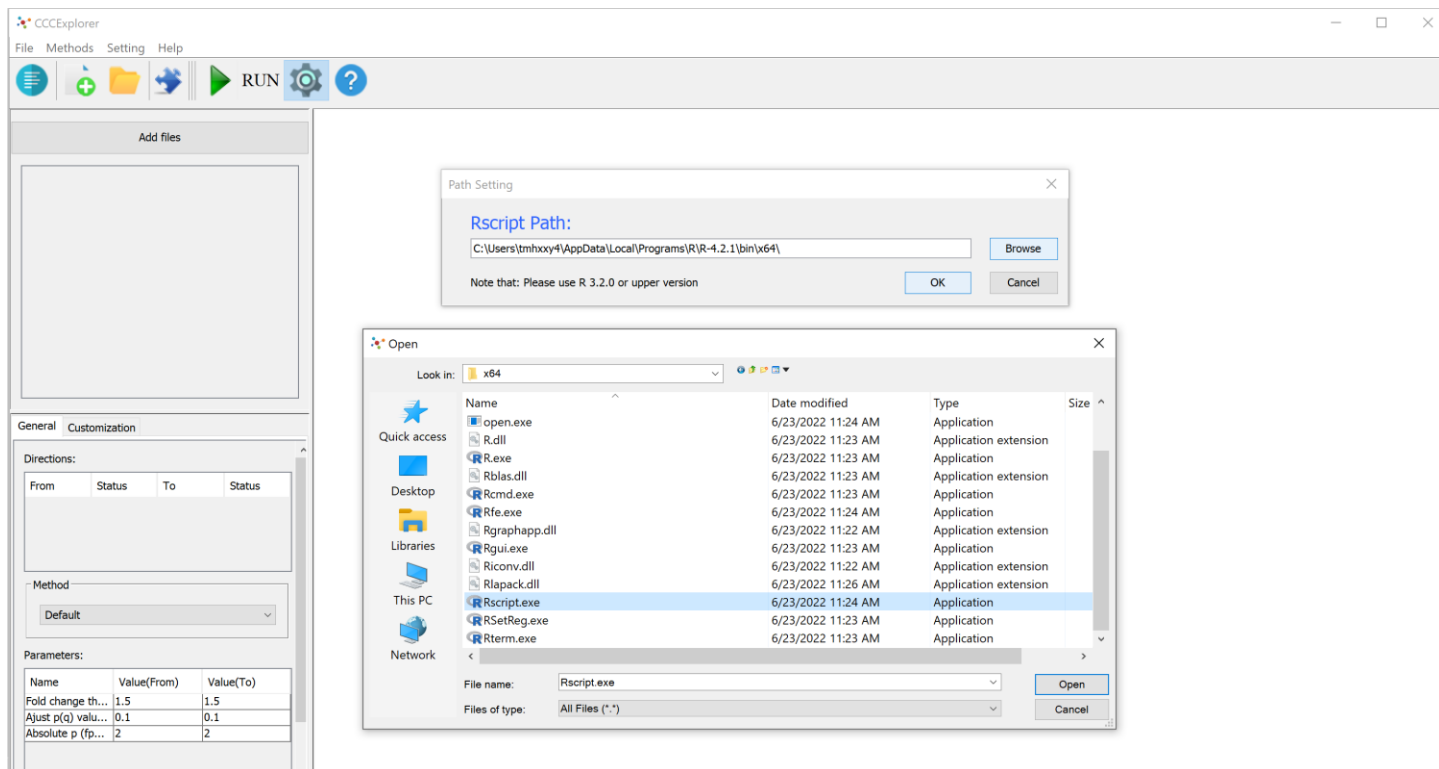


Figure 1

2. How to use CCCExplorer

2.1 Run a project

To run a project, first of all, user needs to select the input files, configure some parameters and choose the specific algorithm program.

User can add multiple cell type files by clicking “Add Files” button, eg. Figure 2. Then select directions like Figure 3.

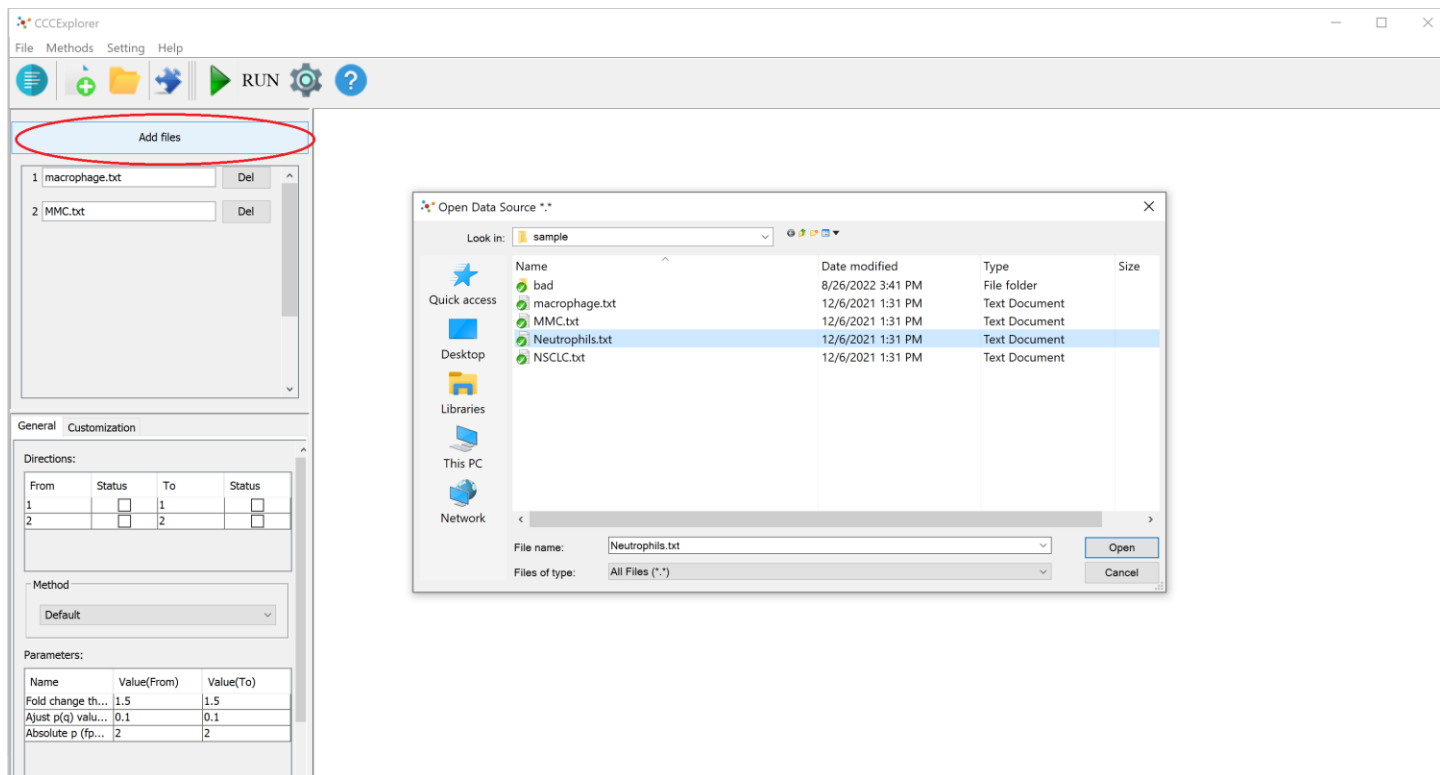


Figure 2

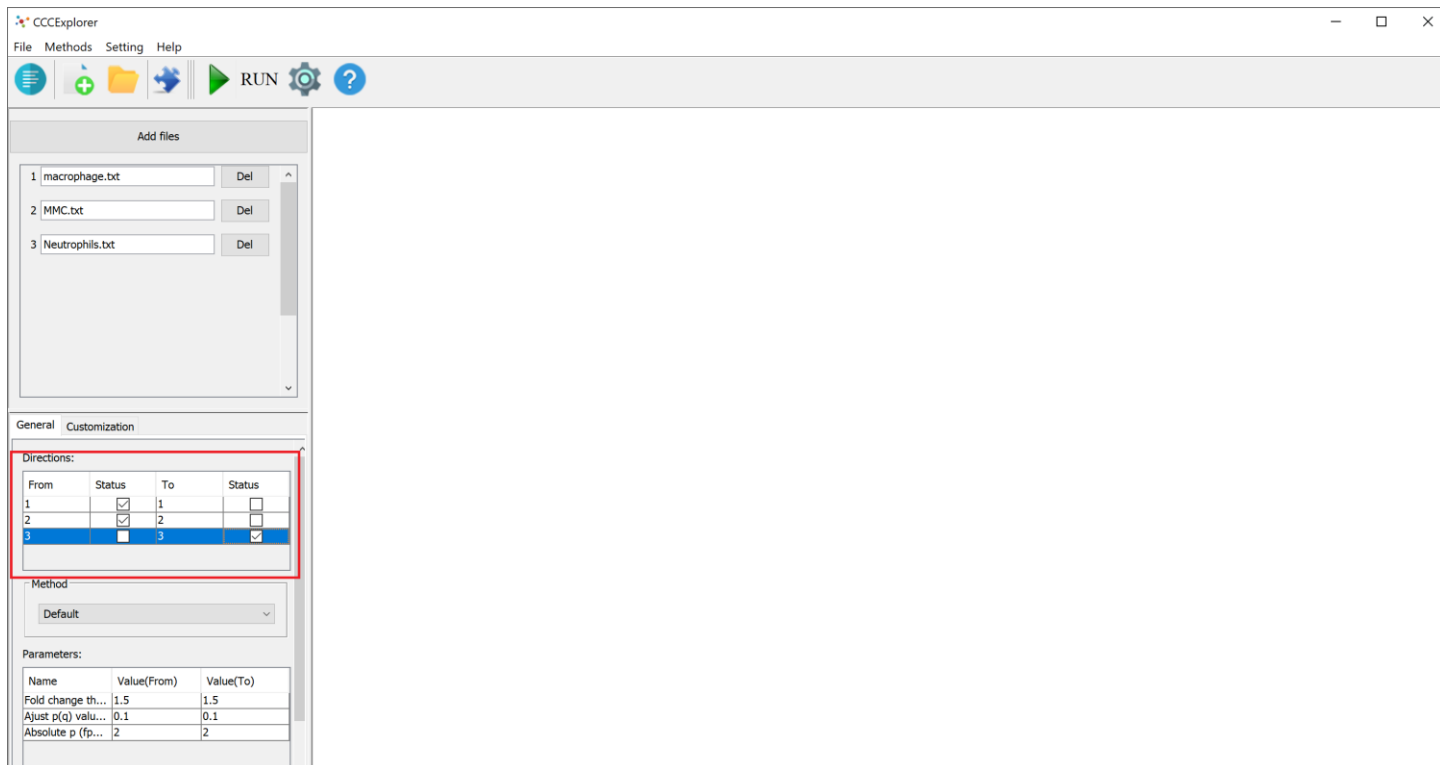


Figure 3

Clicks on “Run” button to run this project. Eg. Figure 4.

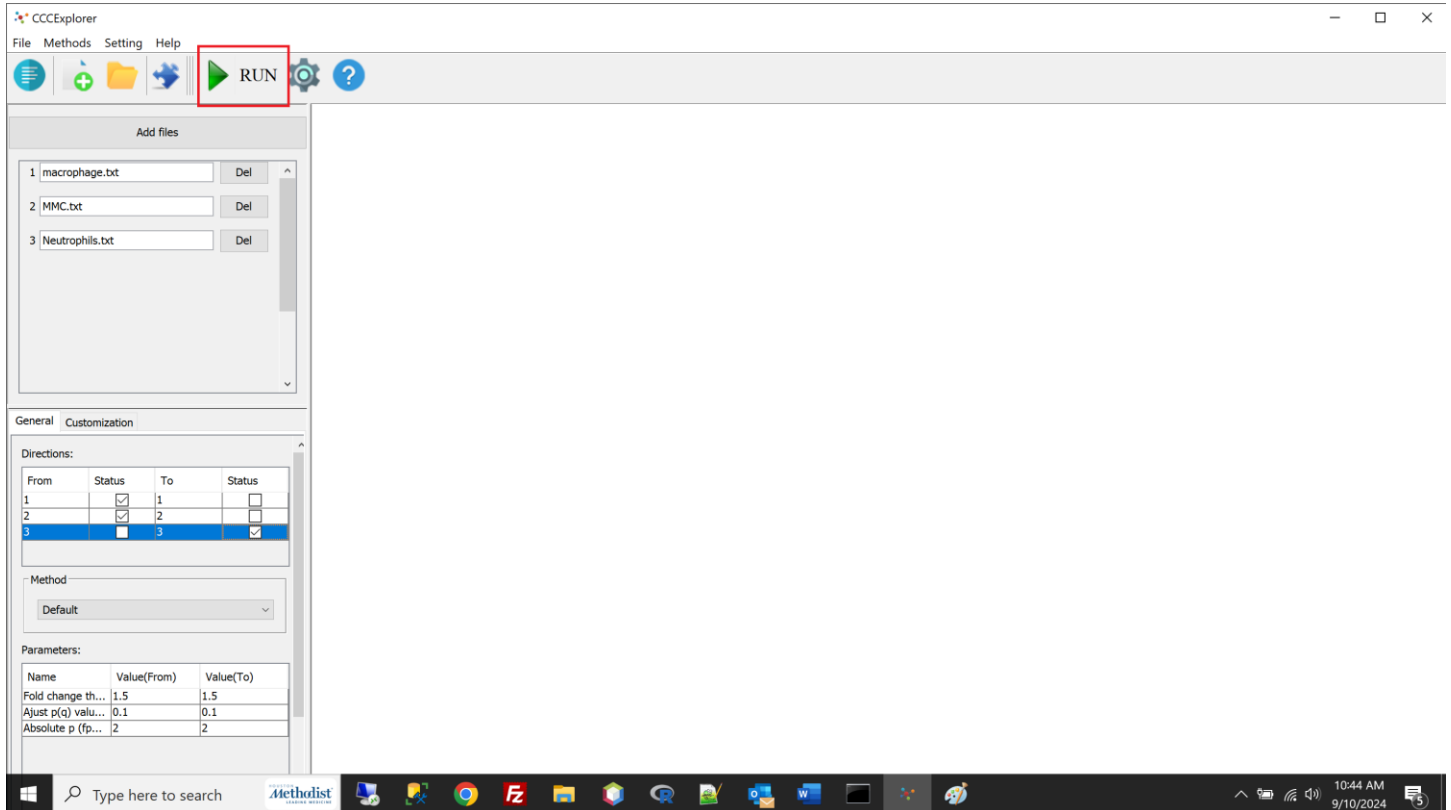


Figure 4

Check the result of a project

When the project is run successfully, there is an overview window will show up as Figure 5. Click the pathways you can open the view of the specific direction.

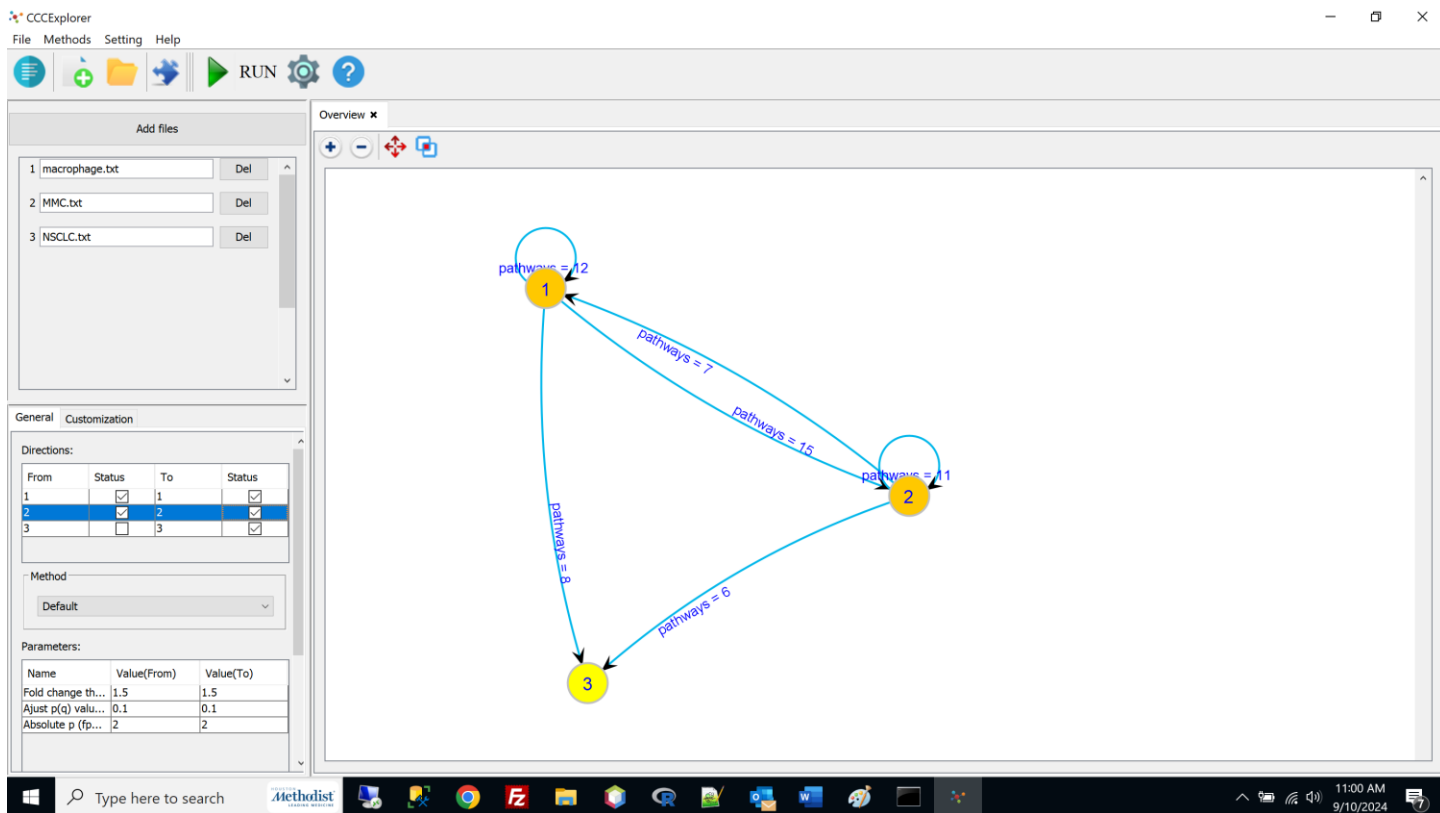


Figure 5

User can check the common pathways and common ligand-receptor pairs by clicking the icon in the Figure 6.

The screenshot displays the CCCExplorer application window. The interface includes a menu bar (File, Methods, Setting, Help), a toolbar with icons for file operations and a 'RUN' button, and a main workspace divided into several panels.

Add files panel: Lists three files: 1. macrophage.txt, 2. MMC.txt, and 3. NSCLC.txt. Each file has a 'Del' button.

General/Customization panel: Contains a 'Directions' table, a 'Method' dropdown set to 'Default', and a 'Parameters' table.

Directions Table:

From	Status	To	Status
1	<input checked="" type="checkbox"/>	1	<input checked="" type="checkbox"/>
2	<input checked="" type="checkbox"/>	2	<input checked="" type="checkbox"/>
3	<input type="checkbox"/>	3	<input checked="" type="checkbox"/>

Parameters Table:

Name	Value(From)	Value(To)
Fold change th...	1.5	1.5
Adjust p(q) valu...	0.1	0.1
Absolute p (fp...	2	2

Overview panel: Features a toolbar with icons for zooming, panning, and exporting, highlighted by a red box.

Common Pathways/Ligand-receptor pairs panel: Contains a table of pathway pairs, a 'Calculate Common Pathways/Ligand Receptor pairs' button (highlighted by a red box), and two lists of results.

Table of Common Pathways/Ligand-receptor pairs:

Select	From Name	To Name	From Index	To Index	Pathway Numbers
<input type="checkbox"/>	macrophage.txt	macrophage.txt	1	1	12
<input checked="" type="checkbox"/>	macrophage.txt	MMC.txt	1	2	15
<input type="checkbox"/>	macrophage.txt	NSCLC.txt	1	3	8
<input checked="" type="checkbox"/>	MMC.txt	macrophage.txt	2	1	7
<input type="checkbox"/>	MMC.txt	MMC.txt	2	2	11
<input type="checkbox"/>	MMC.txt	NSCLC.txt	2	3	6

Common Pathways:

- Osteoclast differentiation
- MAPK signaling pathway
- TNF signaling pathway
- Chemokine signaling pathway
- TGF-beta signaling pathway

Common Ligand/Receptor pairs:

Ligand	Receptor
IL1B	IL1R2
CCL7	CCR5
CXCL1	CXCR2
TNF	TNFRSF1B
TNF	TNFRSF1A
CCL2	CCR1
CCL2	CCR2
CCL2	CCR5

Figure 6

When user click the pathway of the Figure 5, user can see the output details of the selected direction, eg. Figure 7.

The red box 1 in the Figure 5 is the pathway network.

The red box 2 is p value information of pathway.

The red box 3 is the mapping of ligand and receptor.

The red box 4 is the toolbar of output window. User can zoom in, zoom out, invisible pathway and export the pathway.

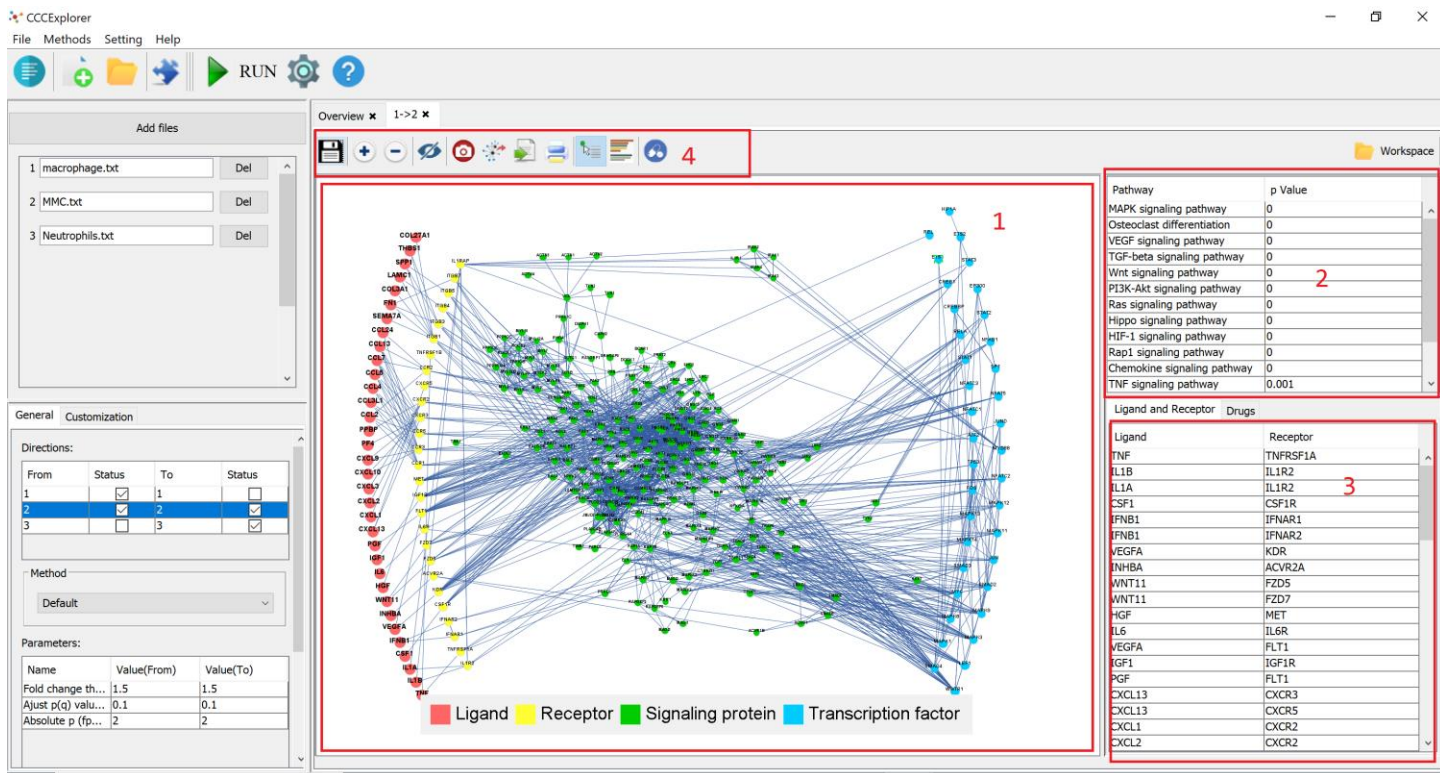


Figure 7

User can right click on a gene node on the pathway network to delete a gene node to see the changes of pathway network. Eg. Figure 8.

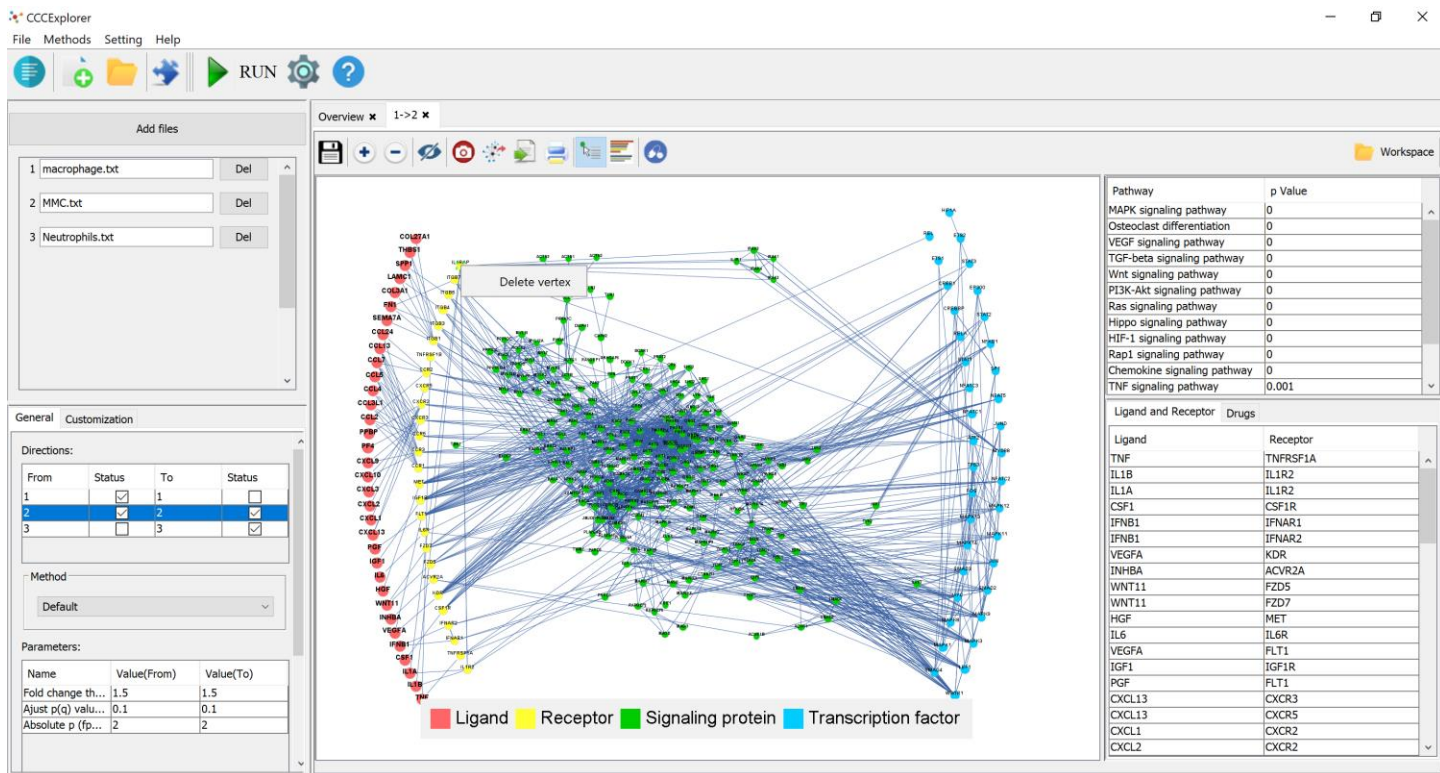


Figure 8

Save a project

To save a project, user can click on the save icon on the toolbar of output window. And then give a project name. Eg. Figure 9.

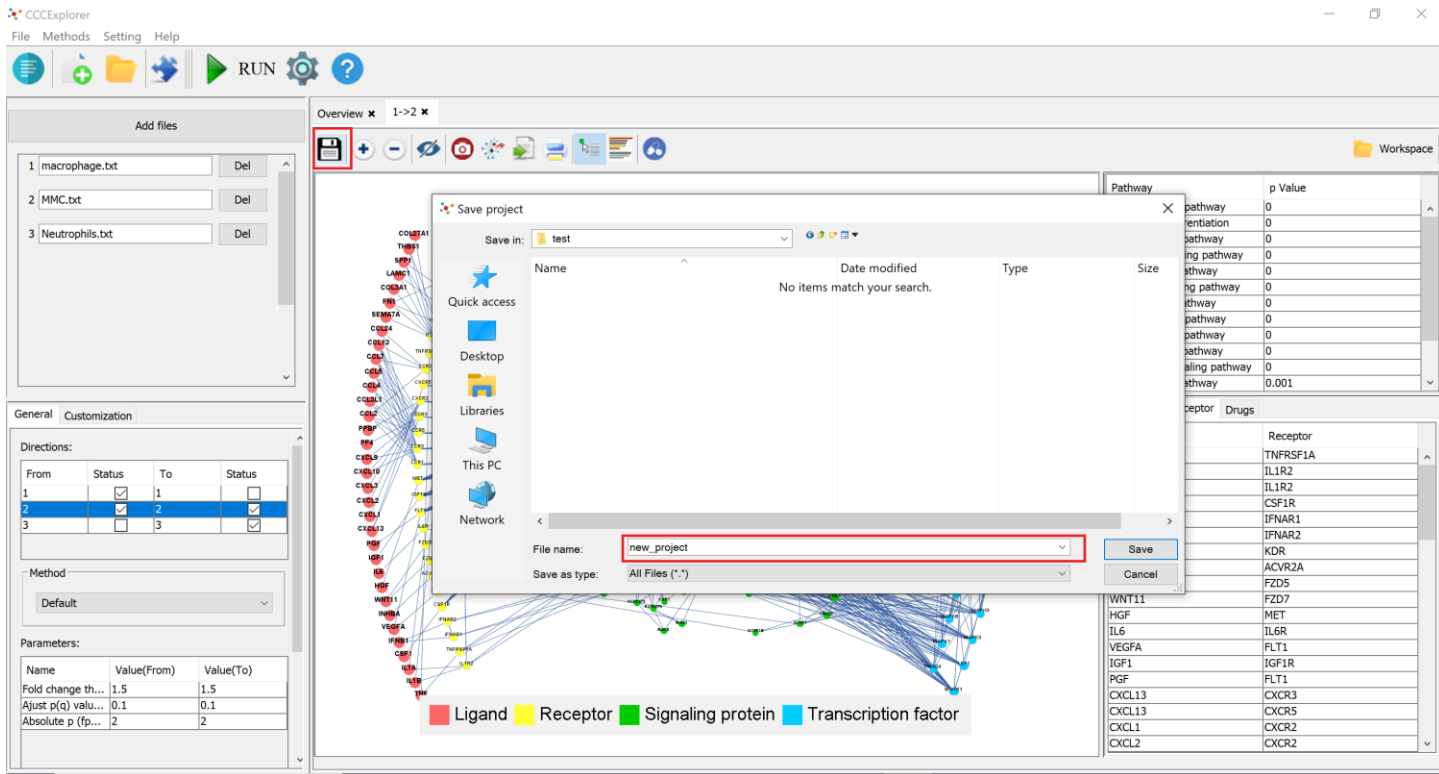


Figure 9

There are several files will be created after clicking save button. The file list is in Figure 10. The .smab file is the project file. User can open this file with CCCExplorer to load a project.

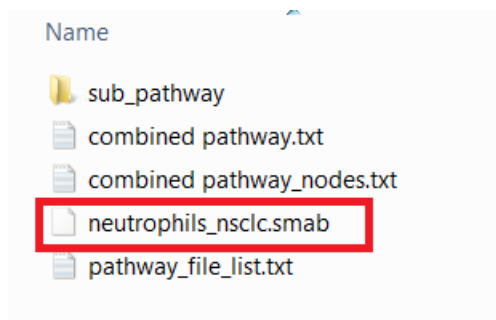


Figure 10

Open an existing project

Clicks on the folder icon on the toolbar of main window and select a project file as figure 11.

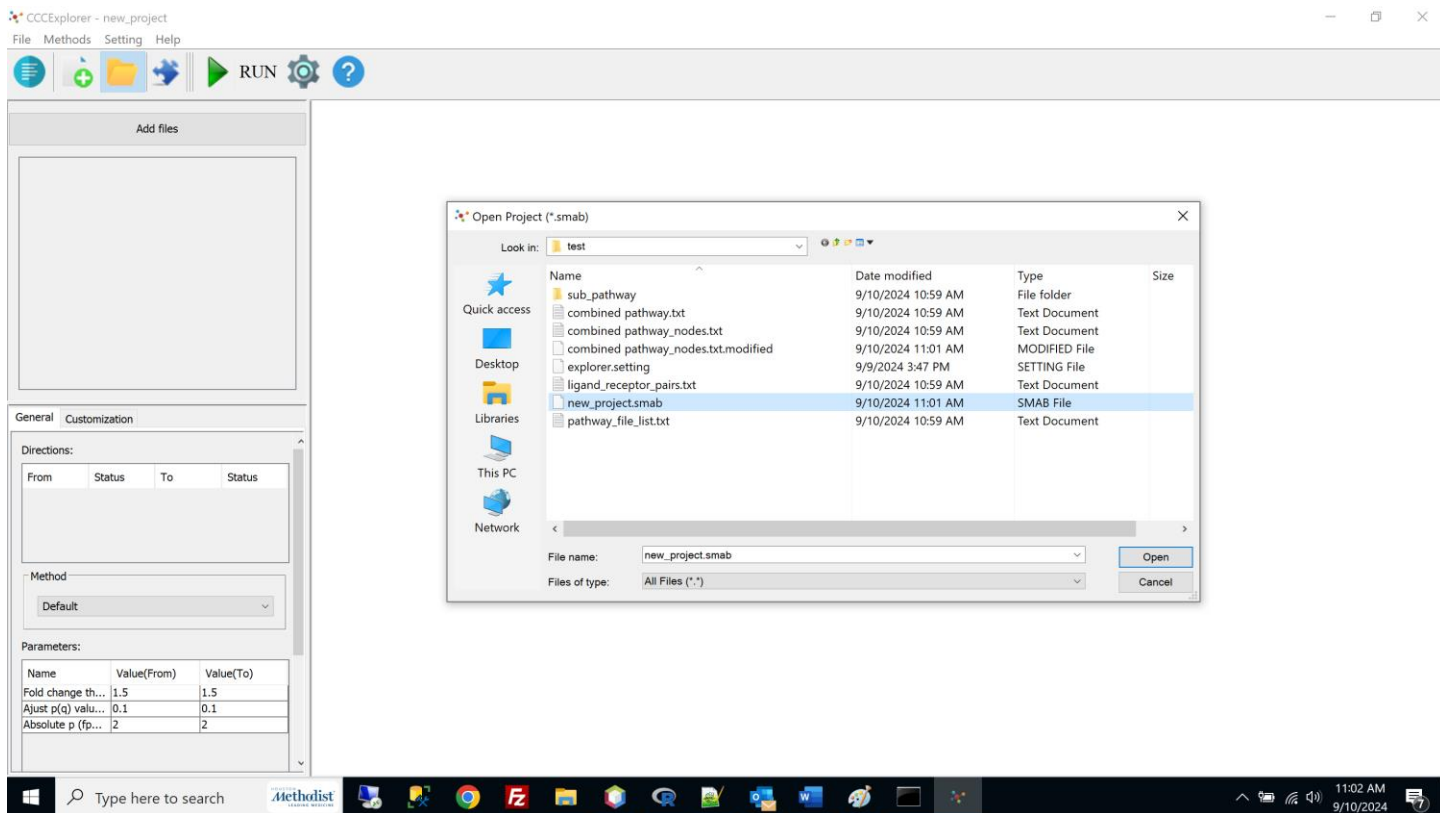


Figure 11

User also can open a project from the recent project list. Click on the first icon on the toolbar of main window to open it.

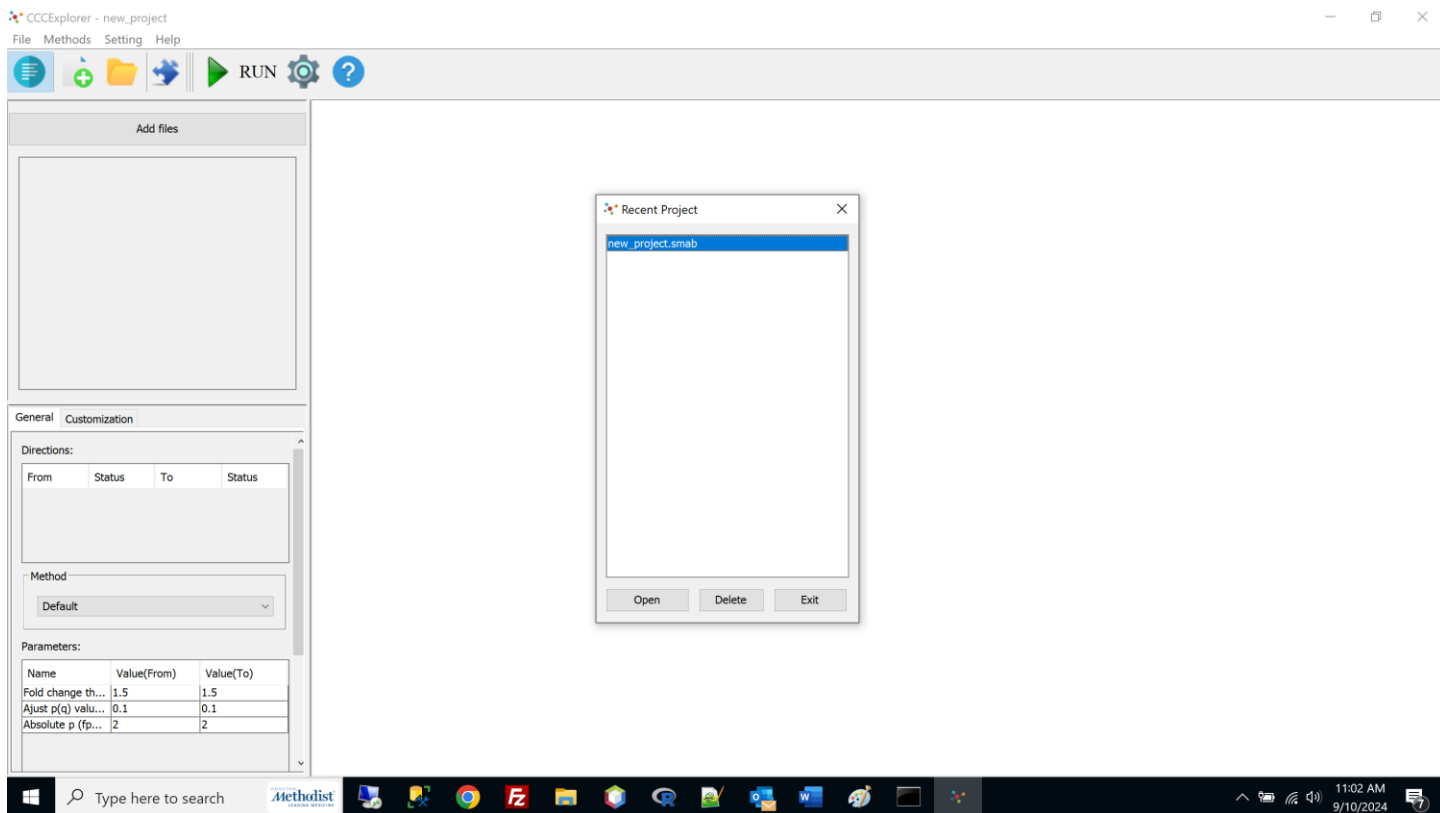
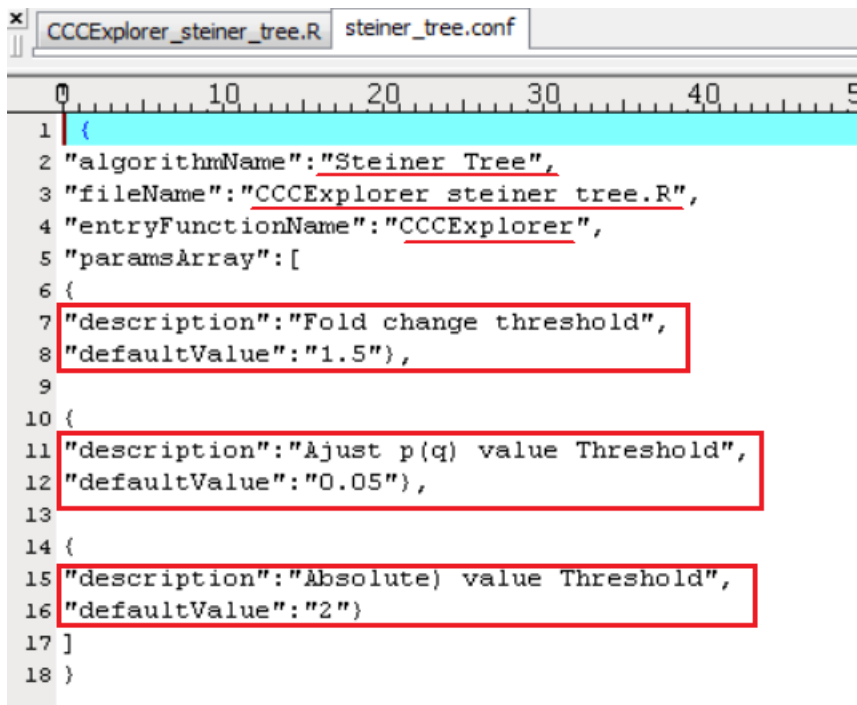


Figure 12

Add a method

To add a new method into CCCExplorer, user needs to provide two files. One is the configuration file, the other is algorithm program. Currently we support the R language based algorithm program. The configuration file is JSON format. User can create a method configuration file according to the interface format of the algorithm file.

The figure 13 is the structure of the configuration file.



```
1 {  
2   "algorithmName": "Steiner Tree",  
3   "fileName": "CCCEXplorer steiner tree.R",  
4   "entryFunctionName": "CCCEXplorer",  
5   "paramsArray": [  
6     {  
7       "description": "Fold change threshold",  
8       "defaultValue": "1.5"},  
9     {  
10      "description": "Adjust p(q) value Threshold",  
11      "defaultValue": "0.05"},  
12      {  
13        "description": "Absolute value Threshold",  
14        "defaultValue": "2"}  
15    ]  
16  }  
17 }  
18 }
```

Figure 13

Figure 14 is the mapping relation between the configuration file and the display UI.

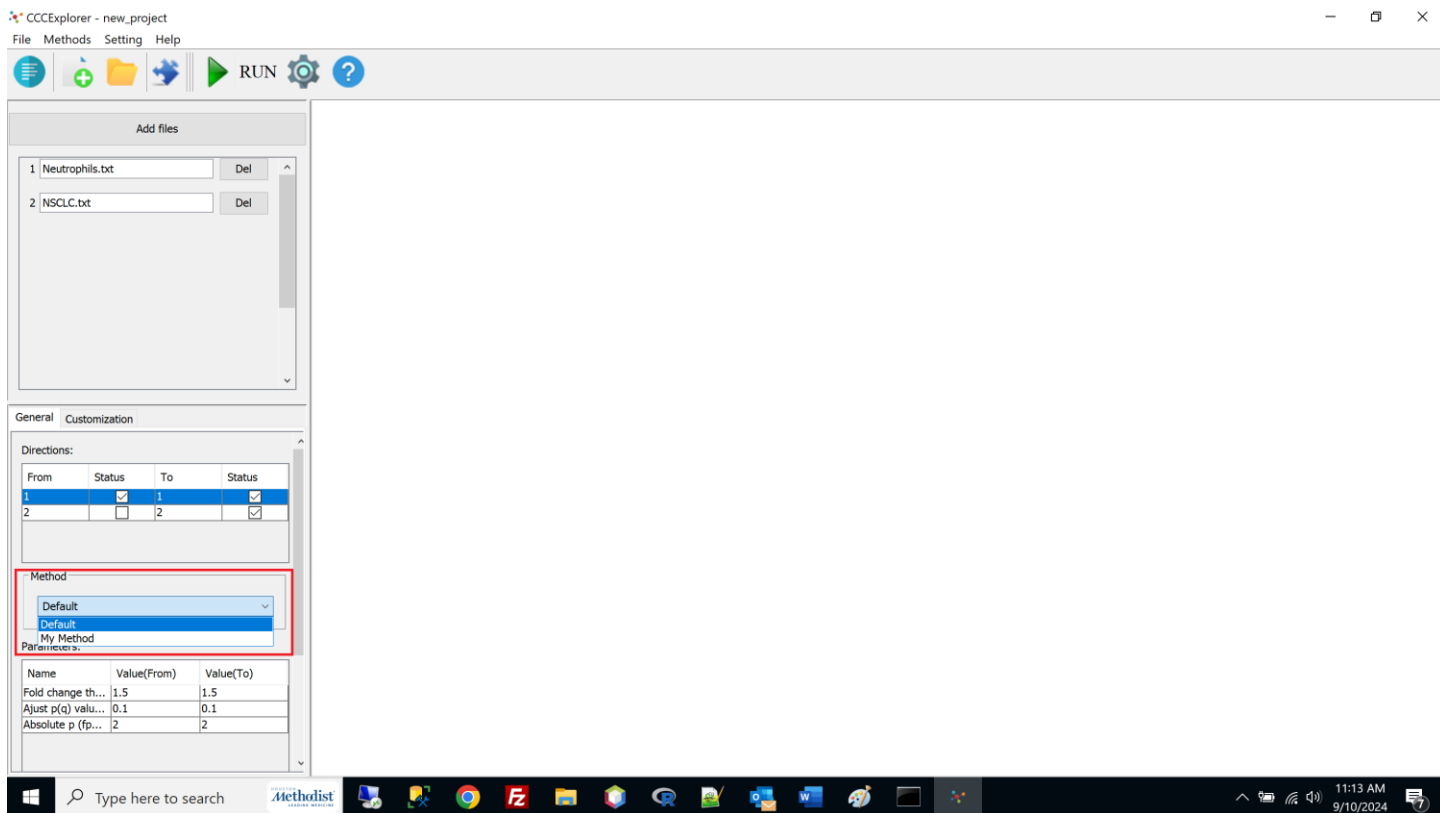


Figure 14

Click on “Methods->Add Method” to select a method configuration file, eg. Figure 15. User needs to make sure the algorithm program is in the same folder as the configuration file.

From the preview box, user can check whether the format of the method is correct.

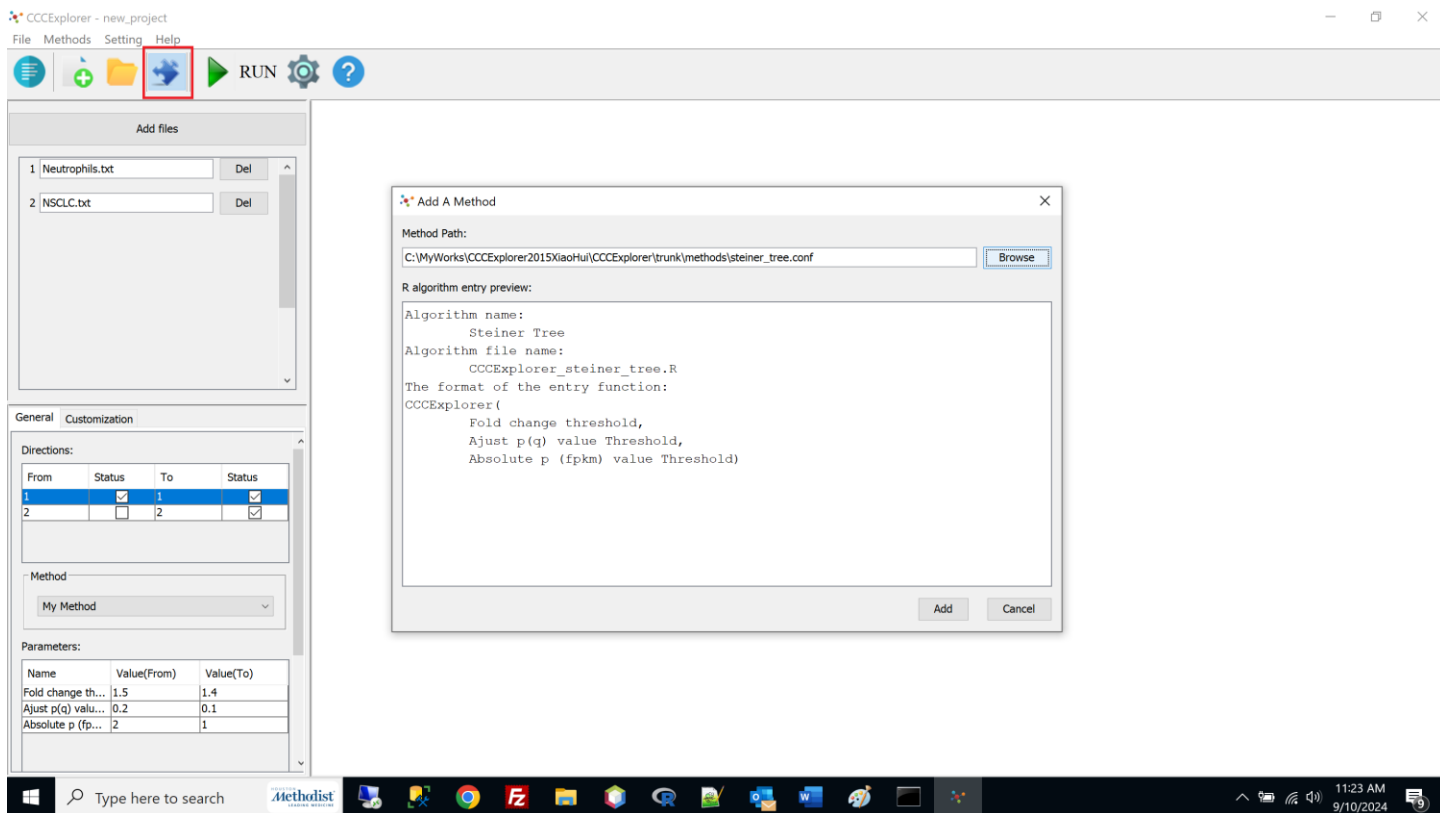


Figure 15

The format of the output files

There are three files and one folder that the algorithm program needs to generate.

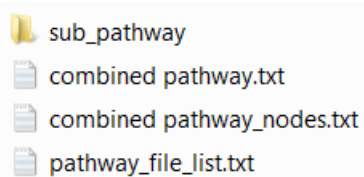


Figure 16

The file "combined pathway.txt" contain the pathway information. The figure below is the format of this file.


```
combined_pathway.txt
0 10 20 30 40
1 From To Direction Interaction_type
2 TNF TNFRSF1A directed LR
3 IL1A IL1R1 directed LR
4 IL1R1 IL1RAP directed heterodimer
5 CHP1 NFATC1 directed process(activation)
```

There are 5 columns in this file. The delimiter of each field is tab character \t.

The file “combined_pathway_nodes.txt” contain the node information. The figure below is the format of this file.

```
combined_pathway_nodes.txt
0 10 20 30 40 50 60 70 80 90
1 gene gene_type pathway
2 NFKB1A links Osteoclast differentiation;TNF signaling pathway;NF-kappa B signaling pathway
3 PLCG2 links Osteoclast differentiation
4 PPP3CA links Osteoclast differentiation
5 PPP3CB links Osteoclast differentiation
6 PPP3CC links Osteoclast differentiation
7 PPP3R1 links Osteoclast differentiation
```

There are 3 columns in this file. The delimiter of each field is tab character \t.

The file “pathway_file_list.txt” contain the sub pathway information. The figure below is the format of this file.

```
pathway_file_list.txt
0 10 20 30 40 50 60 70 80 90 100 1
1 Osteoclast differentiation 0.007 Osteoclast differentiation_nodes.txt Osteoclast differentiation.txt
2 TNF signaling pathway 0.014 TNF signaling pathway_nodes.txt TNF signaling pathway.txt
3 NF-kappa B signaling pathway 0.019 NF-kappa B signaling pathway_nodes.txt NF-kappa B signaling pathway.txt
4 MAPK signaling pathway 0.048 MAPK signaling pathway_nodes.txt MAPK signaling pathway.txt
```

There are 4 columns in this file. The delimiter of each field is tab character \t.

The first column is the name of sub pathway.

The second column is p value.

The third column is the file name of node for sub pathway. It contains the node information of sub pathway.

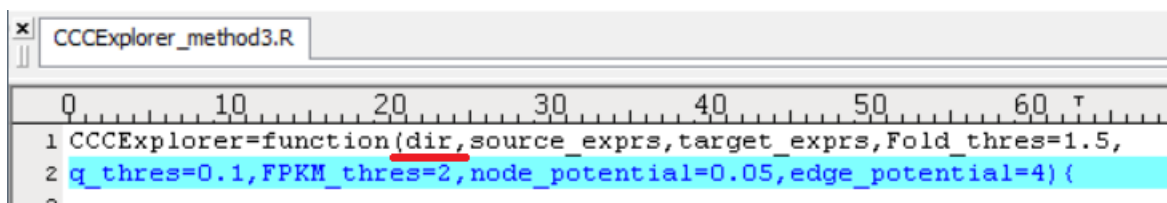
The forth column is the pathway file name of sub pathway. It contains the pathway information of sub pathway.

Algorithm program needs to create a folder named “sub_pathway” and put all the node and pathway information of sub pathway into it.

Note that:

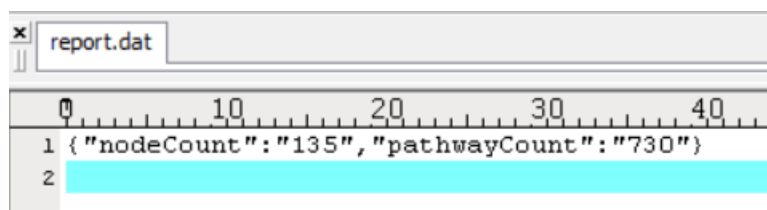
1. The first parameter of the algorithm program is the path in which all the output files will be put.

The figure below is the example of an R algorithm program.



```
1 CCCExplorer=function(dir,source_exprs,target_exprs,Fold_thres=1.5,  
2 q_thres=0.1,FPKM_thres=2,node_potential=0.05,edge_potential=4){  
3
```

2. The algorithm program also needs to create a report file (report.dat) in the current workspace before it returns.
The format of the report file is JSON forma.



```
1 {"nodeCount":"135","pathwayCount":"730"}  
2
```

Drug Discovery

When user clicks drug toggle button, the genes on which has drugs target will be highlighted, eg. Figure 17. User can move the cursor on the drug to see the drug information. When the user moves the cursor between the genes, the drug list will be updated.

To lock the drug list, user needs to double click a drug, then user can double click any drug in the drug list, the CCCExplorer will open the drug-bank website to show the details of this drug.

To unlock the drug list, user only needs to single click any gene.

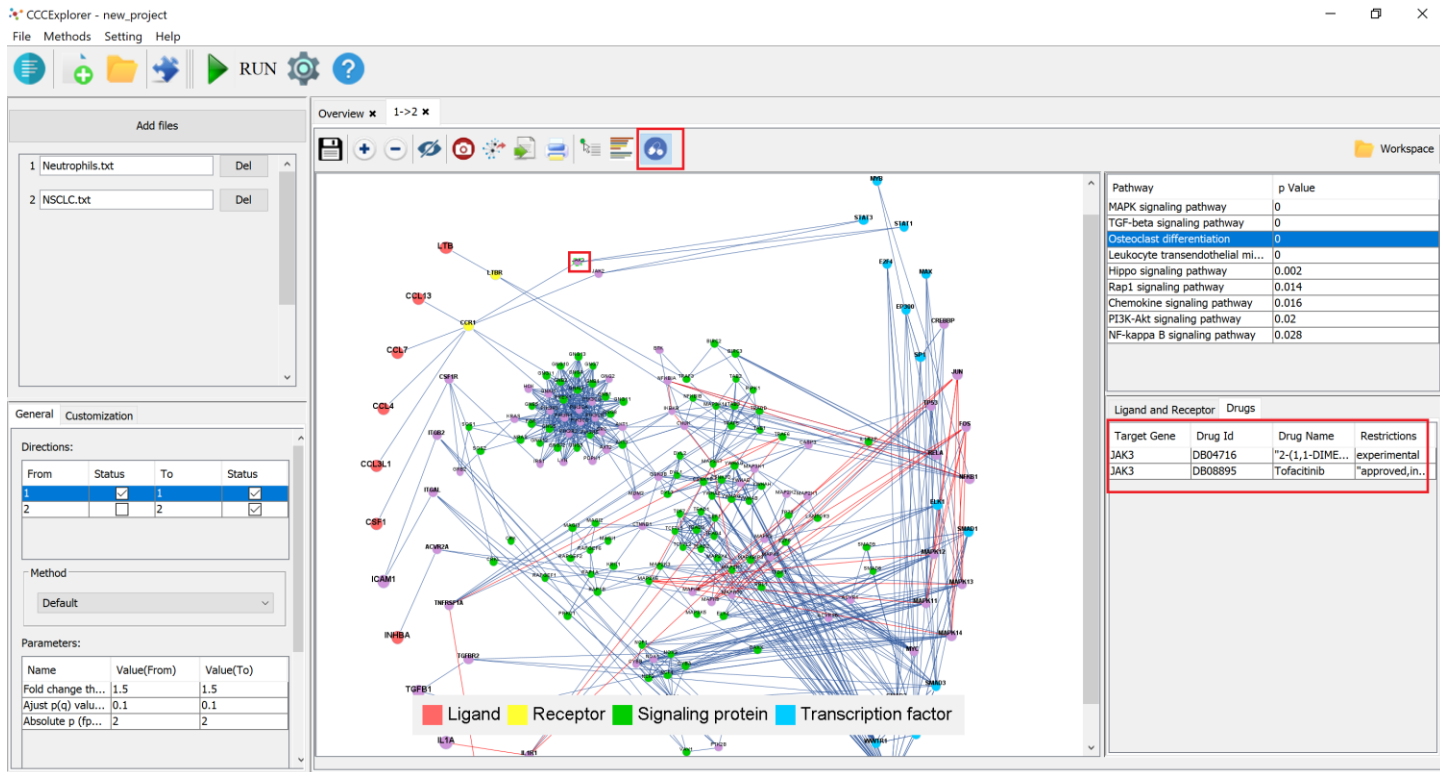


Figure 17