

# manual

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## 1. Overview

Our project aims to design a metabolic platform that simulates changes in the metabolic network to provide comprehensive results for the researcher. You can take the data from our platform, search the pathways between molecules, and perform the metabolic simulations mentioned above.

These functions hosted on the web are divided into three main modules: Synthetic Bay (DB), Pathway Finder (PF), and Deep Metabolic Simulation (DMS). Through

‘/Home’, we can enter the Home page of the project. On this page, users can get our project’s leading content and this manual (Handbook) of the software. At the same time, they can enter the three functional pages by clicking the navigation card.

## 2. Getting start

>> You can input this url ‘/Home’ to visit our web page.

>> ‘Docs’ bar to get this handbook, ‘Git Hub’ bar to visit our Git Hub page to get more code details and Click the white bottom ‘See Illustrations’ you can watch our demonstration video.

Synthesis Navigator

Homepage

Docs

Git Hub

### Come with Synthesis Navigator and sail on the sea of Synthetic Biology!

In this trip, Synthesis Navigator will serve as compass to guide the way. you can get useful metabolic data, design your own metabolic pathway and simulate the metabolic process in the engineered organism.



Get started

See Illustrations

>> The central part of the Home page is these three access interfaces to three function modules. Click on any of the cards, and you can visit our function page.

#### Three steps to construct a complete metabolic pathway

Know -> Practice -> Evaluate



##### Get what you want -Synthetic Bay

Synthetic Bay contains large amounts of metabolic data which can nearly meet all your needs.



##### Search for the best routes -Pathway Finder

We can provide a list of pathways which have been sorted based on the raw material, end-product, and other optional parameters.



##### Evaluate what have been changed -Hybrid Metabolic Simulation

We will simulate almost all of the reactions in the engineered organisms and show the difference before and after the modification.

>> Click the first navigation card from the home page or input ‘/database’ to enter the database module.

>> On the database page, click the blue button ‘Download Data’ to download the data.

## We have built an incredible integrated database of Synthetic Biology for iGEMers & researchers.

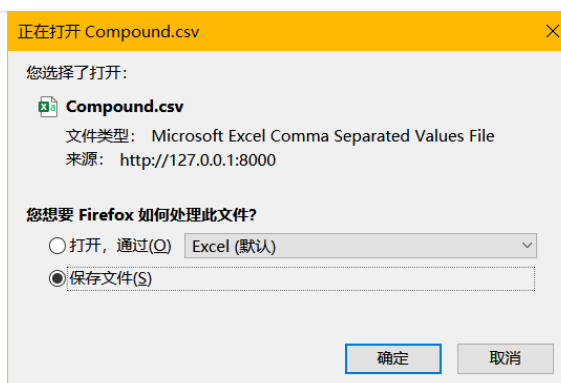
In the Synthetic Bay, you can have a good knowledge of all the compounds, enzymes and reactions which might be significant components of your pathway.

Download Data



>> click each link you want to download. You can download this data. Then you can click the text 'Back to The Home Page' to redirect to the Home page.

[Compound.csv](#)  
[Reaction.csv](#)  
[Enzyme.csv](#)  
[SyntheticBay.db](#)  
[Back to The Home Page](#)



>> Click the second navigation card from the home page or input '/PF' to enter the Pathway Finder module.

>> In the forward pathway finder, you can input a start compound and an end compound, and we will search the pathway from start to end and rank them by scores.

## Pathway Finder

### 1. Search form start compound to the target

input start and end compound

C06033

C06034

>> There are five parameters: KM, KKM, Toxicity, PH, Temperature. You can assign value to the five parameters according to their importance in the experimental environment or your prior knowledge.

set your weight of the pathway ranking, including KM(Michaelis constant), KKM(Kcat/Km), toxicity, PH and tempreature

0.2	0.6	0.2
0.2	0.2	

>> Click the search button, you will get a PDF result, and you can download it.

## Pathway Finder

### 1. Search form start compound to the target

input start and end compound

C06033	C06034
--------	--------

set your weight of the pathway ranking, including KM(Michaelis constant), KKM(Kcat/Km), toxicity, PH and tempreature

0.2	0.6	0.2
0.2	0.2	

Search

[pathway\\_res\\_2020\\_10\\_24\\_65507017.pdf](#)  
[Back to The Home Page](#)

>> You should input the target compound A and the search depth——steps B to get the pathway target to A with Steps no more than B. Click the search button, and you will get a similar PDF file.

### 2. Reverse Search from the end compound

C06034	4
--------	---

Search

>> Click the third navigation card on the home page or '/HMS' to enter the Deep Metabolic Simulation module.

>> you should input the observation\_list first, which is the compound you want to observe, and we will show them in the top of the results with red color.

Observation list: C00018;C00075;C00322

>> second, in delete\_reaction\_list, You can delete some reactions to block the paths between molecules.

Delete reactions: R00018

>> you should enter two default values. The first is an initial default value of all the compounds, we will define the compounds' amount with this number, and the second is the iteration times our algorithm will go through.

default value:  default epoches:

>> At the last, the most critical parameter is specified\_values. You can define every specified compound with an initial value, and we will replace this compound's default value with it.

The specified value of compounds:

>> When you input all the parameters, you can click the RUN DMS button to run the algorithm. You may need to wait some minutes, and then you can get two results.

**DMS(Deep Metabolic Simulation)**

Observation list:

Delete reactions:

default value:  default epoches:

The specified value of compounds:

>> One is a PDF file in which we show the compounds in observation\_list and whose value's change is in rank TOP50, the other one is CSV file, we output all the change information of all compounds.

---

[randomwalk\\_res\\_2020\\_10\\_24\\_98104347.pdf](#)  
[randomwalk\\_res\\_2020\\_10\\_24\\_98104347.csv](#)  
[Back to The Home Page](#)

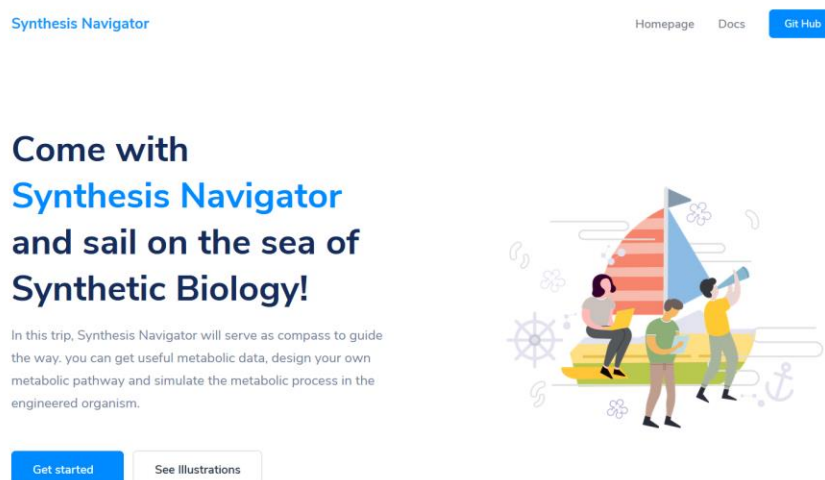
## 3. Details about our software

### Home and handbook

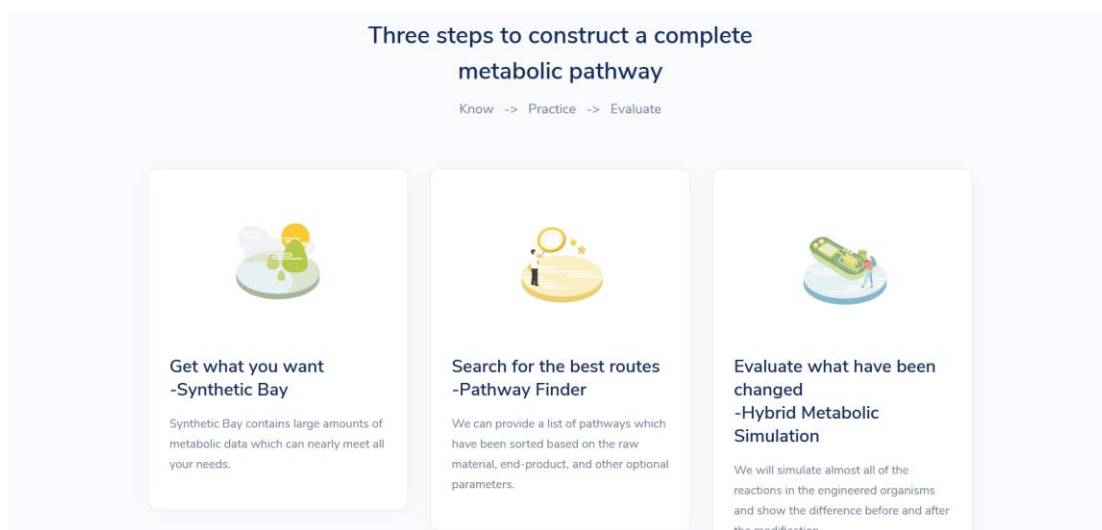
On this page, you can see a brief introduction to our project. And on the top of this page, there are three navigator bars you can click to visit. 'Homepage' bar to redirect to the Home page, 'Docs' bar to get this handbook, and 'Git Hub' bar to see our Git Hub page to get more code details.

Under the overview text, you can see two bottoms colored with blue and white, respectively. Click the white button, and you can watch our demonstration video, in

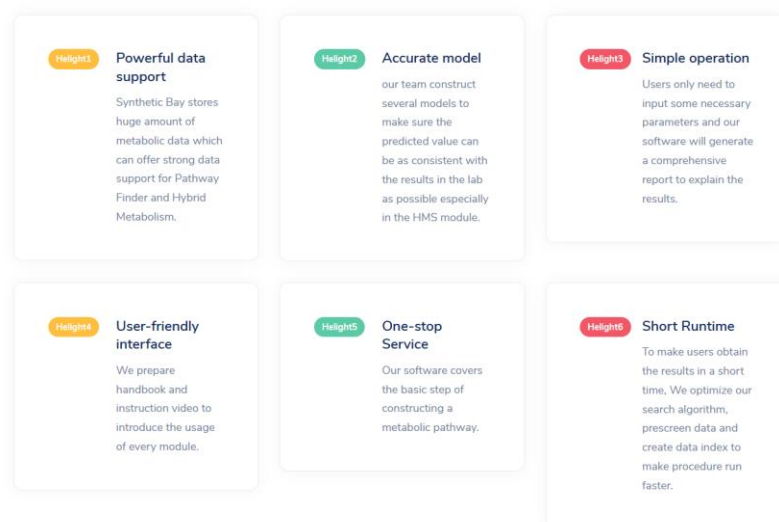
which we show how to use our function modules.



The central part of the Home page is these three access interfaces to three function modules. Click on any of the cards, and you can visit our function page.



Meanwhile, we have summarized six advantages in the bottom: Powerful database, Accurate models, Simple operation, User-friendly interface, One-stop service and Short Runtime. You can read more conclusions about our software on the Home page.



## Synthetic Bay

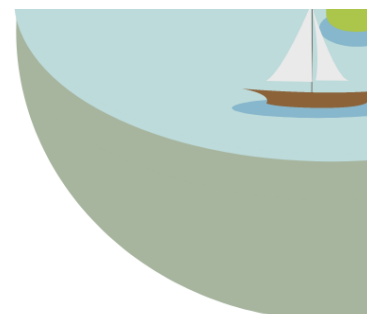
### ● About pages

Click the navigation card from the home page or input ‘/database’ to enter the database module.

Here, you will know the basic framework of our data and download the data. Our data provides four downloadable files, named “reaction.csv”, “compound.csv”, “enzyme.csv” and “SyntheticBay.db”, respectively.

In the Synthetic Bay, you can have a good knowledge of all the compounds, enzymes and reactions which might be significant components of your pathway.

[Download Data](#)



### ● About database

To provide data support for the Synthesis Navigator software’s pathway search function and metabolic simulation function, we integrated several databases, including MetaCyc, ChEBI, BRENDA, eQuilibrator, and KEGG. Finally, we have constructed a database in *sqlite* and *sql* form, in which we create three tables: compounds, reactions and enzymes.

Compounds data is integrated from KEGG and ChEBI. We have selected 1.8k compound entries, include the information about KEGG id, compound name, formula, smile, toxicity, molecule mass, and sdf string.

**Smile:** a 2D pattern of molecules that can show you the structure of these molecules.

**Toxicity:** The value is associated with high or low toxicity of this compound. When it has high toxicity, it will be harmful to biological chassis.

**Sdf string:** a 3D pattern involves the spatial position of every atom.

```
cid,name,formula,smile,toxicity,weight,sdf
C00001,water,H2O,O,,18.0153,' Marvin 01211112152D 3 2 0 0 0 0
C00002,ATP,C10H16N5O13P3,Nc1ncnc2c1ncn2[C@@H]1O[C@H](COP(=O)(O)OP(=O)(O)OP(=O)(O)O)[C@H](O)[C@@H](O)[C@@H]1O
C00003,NAD(+),C21H28N7O14P2,NC(=O)C1CCC[n+](C1)[C@@H]2O[C@H](COP(=O)(O)OP(=O)(O)OC[C@H]3C[C@@H](O)[C@@H](O)[C@@H]3O)[C@H](O)[C@@H]2O
C00004,NADH,C21H29N7O14P2,NC(=O)C1CCN([C@@H]2O[C@H](COP(=O)(O)OP(=O)(O)OC[C@H]3O[C@H](O)[C@@H](O)[C@@H]3O)[C@H](O)[C@@H]2O)[C@H](O)[C@@H]1O
C00005,NADPH,C21H31N7O14P3,NC(=O)C1CCN([C@@H]2O[C@H](COP(=O)(O)OP(=O)(O)OC[C@H]3O[C@H](O)[C@@H](O)[C@@H]3O)[C@H](O)[C@@H]2O)[C@H](O)[C@@H]1O
C00006,NADP(+),C21H29N7O14P2,NC(=O)C1CCC[n+](C1)[C@@H]2O[C@H](COP(=O)(O)OP(=O)(O)OC[C@H]3C[C@@H](O)[C@@H](O)[C@@H]3O)[C@H](O)[C@@H]2O
C00007,dioxygen,O2,O=O,,31.9988,' Marvin 02030822342D 2 1 0 0 0 0
C00008,ADP,C10H15N5O10P2,Nc1ncnc2c1ncn2[C@@H]1O[C@H](COP(=O)(O)OP(=O)(O)O)[C@H](O)[C@@H](O)[C@@H]1O
C00009,phosphate(3-),O4P,O=P([O-])([O-])[O-],,94.97136,' Marvin 10300609012D
C00010,coenzyme A,C21H36N7O16P3S,CC(C)(COP(=O)(O)OP(=O)(O)OC[C@H]1O[C@H](n2cnc3c(N)nc(C)nc32)C[C@H](O)[C@@H](O)[C@@H]1O)C[C@H](O)[C@@H](O)[C@@H]2O
C00011,carbon dioxide,CO2,O=C=O,,44.01,' Marvin 10290522252D 3 2 0 0
C00012,peptide,(C2H2NOR)nC2H3NOR,*C(N)C(=O)NC(*)C(=O)O,,, Marvin 07051116182D
C00013,diphosphate(4-),O7P2,O=P([O-])([O-])OP(=O)([O-])[O-],,173.94332,' Marvin 1205
C00014,ammonia,H3N,N,,17.03056,' Marvin 09260512442D 4 3 0 0 0 0
C00015,UDP,C9H14N2O12P2,O=c1ccn([C@@H]2O[C@H](COP(=O)(O)OP(=O)(O)O)[C@H](O)[C@@H](O)[C@@H]2O)c(C1=NC=CC=C1)[C@H](O)[C@@H](O)[C@@H]1O
C00016,FAD,C27H33N9O15P2,Cc1cc2nc3c(=O)[nH]c(=O)nc-3n(C[C@H](O)[C@H](O)[C@H](O)COP(=O)(O)OP(=O)(O)OP(=O)(O)O)c2cc1)C[C@H](O)[C@@H](O)[C@@H]3O
C00017,protein polypeptide chain,,,,
C00018,pyridoxal 5'-phosphate,C8H10NO6P,Cc1ncc(COP(=O)(O)O)c(C=O)c1O,,247.1419,' Marv
C00019,S-adenosyl-L-methionine,C15H23N6O5S,C[S+](CC[C@H](N)C(=O)O)C[C@H]1O[C@H](n2cnc(C)nc2)C[C@H](O)[C@@H](O)[C@@H]1O
C00020,adenosine 5'-monophosphate,C10H14N5O7P,Nc1ncnc2c1ncn2[C@@H]1O[C@H](COP(=O)(O)O)[C@H](O)[C@@H](O)[C@@H]1O
C00021,S-adenosyl-L-homocysteine,C14H20N6O5S,Nc1ncnc2c1ncn2[C@@H]1O[C@H](CSCC[C@H](N)C(=O)O)[C@H](O)[C@@H](O)[C@@H]1O
C00022,pyruvate,C3H3O3,CC(=O)C(=O)[O-],,87.05412,' Marvin 11220615062D 6
```

Reaction data is collected from KEGG, including above 10k rows. This data table has record six features of reactions: KEGG id, EC number of enzymes participate in the reaction, equation of reaction, reaction class, Gibbs energy from the experiment, frequency of the reaction.

```
rid,ecnum,equation,reactionclass,energy,frequency
R00002,1.18.6.1,16 C00002 + 16 C00001 + 8 C00138 <=> 8 C05359 + 16 C00009 + 16 C00000
R00004,3.6.1.1,C00013 + C00001 <=> 2 C00009,, -15.8 0.4,
R00005,3.5.1.54,C01010 + C00001 <=> 2 C00011 + 2 C00014,C00011_C01010,-78.5 15.1,
R00006,2.2.1.6,C00900 + C00011 <=> 2 C00022,C00022_C00900,32.3 7.4,
R00008,4.1.3.17,C06033 <=> 2 C00022,C00022_C06033,16.3 4.6,
R00009,1.11.1.6 1.11.1.21,2 C00027 <=> C00007 + 2 C00001,C00007_C00027,-193.1 13.3
R00010,3.2.1.28,C01083 + C00001 <=> 2 C00031,C00031_C01083,-11.7 2.1,
R00011,1.11.1.13 1.11.1.16,2 C19610 + C00027 + 2 C00080 <=> 2 C19611 + 2 C00001,,1
R00012,2.7.7.45,2 C00044 <=> C00013 + C01261,C00044_C01261,nan nan,
R00013,4.1.1.47,2 C00048 <=> C01146 + C00011,C00048_C01146,-19.6 8.8,
R00014,1.2.4.1 2.2.1.6 4.1.1.1,C00022 + C00068 <=> C05125 + C00011,C00068_C05125
R00015,2.4.1.99,2 C00089 <=> C00031 + C03661,C00031_C00089 C00089_C03661,-6.1 10.7
R00017,1.11.1.5,C00027 + 2 C00126 <=> 2 C00125 + 2 C00001,C00125_C00126,nan nan,
R00018,2.5.1.44,2 C00134 <=> C06366 + C00014,C00134_C06366,-0.9 8.0,
R00019,1.12.7.2 1.12.99.-,2 C00138 + 2 C00080 <=> C00282 + 2 C00139,,18.0 13.0,
R00021,1.4.7.1,2 C00025 + 2 C00139 <=> C00064 + C00026 + 2 C00138 + 2 C00080,C00025_
R00022,3.2.1.52,C01674 + C00001 <=> 2 C00140,C00140_C01674,-13.8 10.8,
R00023,1.7.1.5,2 C00192 + 2 C00003 <=> C01818 + 2 C00004 + 2 C00080,C00003_C00004,nan
R00024,4.1.1.39,C01182 + C00011 + C00001 <=> 2 C00197,C00197_C01182,-28.4 7.5,
R00025,1.13.12.16,C18091 + C00007 + C01847 <=> C00084 + C00088 + C00061 + C00001,C00
R00026,3.2.1.21,C00185 + C00001 <=> 2 C00221,C00185_C00221,-12.9 3.7,
R00027,4.1.2.38,C01408 <=> 2 C00261,C00261_C01408,7.8 10.2,
```

Enzyme data is gathered from KEGG, BRENDA, and eQuilibrator. This data is too big to load because of its 28k items and also 14 columns. We try to include more comprehensive enzyme information and use them for pathway finding. We will show you the meaning of these features below:

**PID:** protein id corresponds to the sequence.

**name:** enzyme name.



ecnum: EC number.

organism: chassis.

Localization: the position where the enzyme is located in the cell.

pH & pHr: *Pondus Hydrogenii*, pH and pH range for normal enzyme function.

T & Tr: temperature and temperature range for normal enzyme function.

KM: Michaelis constant.

KKM: Kcat/Km.

sequence: the protein sequence of enzyme.

pid	name	ecnum	organism	localization	ph	pHr	t	tr	km	kkm	sequence
P43309	catechol oxidase	1.10.3.1	Malus domestica	membrane	6.5	#6.8, 2.5-9	20	#30, 20-80			
O81103	catechol oxidase	1.10.3.1	Prunus armeniaca								MATAPSPPTMGTYSSLISTNSFSTFLPNK
P43311	catechol oxidase	1.10.3.1	Vitis vinifera		5		25				MASLPWSLTSTAIANTTNISAFPPSP
Q9MB14	catechol oxidase	1.10.3.1	Ipomoea batatas						-999	{more}	#9 {catechol}#3.9 {4-
Q08303	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			MASLCSNS
Q08304	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			MASVVCNS
Q06355	catechol oxidase	1.10.3.1	Solanum tuberosum		6.5		25		21.1	{catechol}	SSSSTTI
Q9ZP19	catechol oxidase	1.10.3.1	Ipomoea batatas						-999	{more}	#9 {catechol}#3.9 {4-
Q08305	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			MASLCSNS
Q08306	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			MASLCSNS
Q08307	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			MSSSSIT
Q08296	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			MSSSTPNT
B3VQ03	catechol oxidase	1.10.3.1	Camellia sinensis		5.3	5.7					MASILPPTTKTTTSSTLYS
B5M677	catechol oxidase	1.10.3.1	Ipomoea batatas						-999	{more}	#9 {catechol}#3.9 {4-
A6N8J4	catechol oxidase	1.10.3.1	Camellia sinensis		5.3	5.7					MASILPPTTKTTTSSTLYS
O24057	catechol oxidase	1.10.3.1	Malus domestica	membrane	6.5	#6.8, 2.5-9	20	#30, 20-80			
Q5ENY2	catechol oxidase	1.10.3.1	Ipomoea batatas						-999	{more}	#9 {catechol}#3.9 {4-
D6QY28	catechol oxidase	1.10.3.1	Solanum melongena								MASVCNTSTATLKSSFIPSPNSLGSTPK
Q6ZXV3	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			YGVANAIP
B5M678	catechol oxidase	1.10.3.1	Ipomoea batatas						-999	{more}	#9 {catechol}#3.9 {4-
B5M680	catechol oxidase	1.10.3.1	Ipomoea batatas						-999	{more}	#9 {catechol}#3.9 {4-
Q6ZXV2	catechol oxidase	1.10.3.1	Solanum lycopersicum		4.8	4.1-4.4	40	30-50			DIQNKDWL

## ● About results

You can download three tables data in the form of the '.csv' file and one database in the '.db' file format.

Three tables data is split with ',' and you can read the information with Excel or Text Reader (Notepad++). This form is convenient for data analysis, manage with commands and other pipelines. The database can be used with SQL commands or SQL software (MySQL, SQL server).



- About page

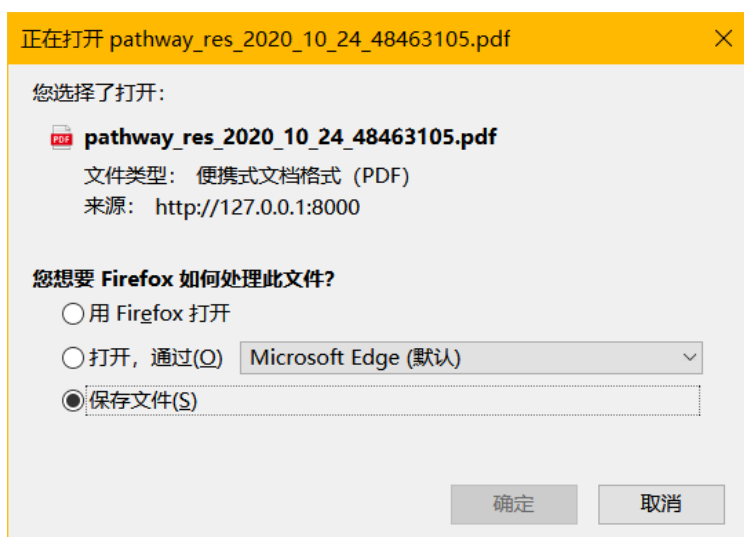
Click the navigation card on the home page or '/PF' to enter the Pathway Finder module.

In the middle of this page, you can find one gray window consist of many entry bars. It is the central part of the pathway finder, including two functions: forward pathway search and reverse pathway search.

In the first function, you can input a start compound and an end compound. We will search for the pathways from start to end and rank them by scores. There are five parameters: KM, KKM, Toxicity, PH, Temperature. You can assign value to the five parameters according to their importance in the experimental environment or your prior knowledge. Click the search button, you will get PDF results, and you can download this PDF.

[pathway\\_res\\_2020\\_10\\_24\\_71893992.pdf](#)

[Back to The Home Page](#)



The reverse pathway search is very much like the forward. It would help if you inputted the target compound a and the search depth——steps b to get the pathway target to a with Steps no more than b. And click the search button, you will get a similar PDF file

## 2. Reverse Search from the end compound

- About functions

The core of our Pathway Finder is traditional graph algorithms. A\*, Dijkstra, and Yen's k shortest way algorithm are used.

Forward pathway search function, According to the length of the path (energy score of reactions) and weighted score, will calculate scores and sort all the pathways between the start and end compound to output the better pathways (TOP10) and their scores.

Weighting score is computed by the five features (KM, KKM, Toxicity, PH, temperature) and user's weight ratio, which is entered by you through the five parameters input bar. These five ratio parameters mean the weight ratio of the feature's influence. A weight matrix will be created based on the value you input and the content of data, and then a score will be given to these pathways.

In the reverse pathway search, you will get some pathways that can produce the target molecule no more than the number of steps you input. The scores of these pathways will be presented to you, too.

- About results

We will show you a download link for our results. The results are output in PDF format and divided into two parts: Summary and Results.

### PythwayFinder

#### Summary:

start\_compound: C06033  
end\_compound: C06034  
km = 0.2; kkm = 2.0; Toxi = 3.0; PH = 0.2; temp = 0.2;

#### Results:

4-hydroxy-4-methyl-2-oxoglutaric acid——(R05077,)——>4-hydroxy-4-methylglutamate  
EnergyScore: 3034.9 IndiScore: 1.0

The summary part concludes all the parameters, through which you can know what you have input and what you want to get. In the forward pathway finder, you see the start\_compound and end\_compound, but in the reverse pathway finder, you can see the target (end\_compound).

## PythwayFinder

### Summary:

end\_compound: C06034  
km = 0.2; kkm = 0.2; Toxi = 0.2; PH = 0.2; temp = 0.2;  
steps = 4

### Results:

start\_Compound:4-hydroxy-4-methyl-2-oxoglutaric acid ||  
4-hydroxy-4-methyl-2-oxoglutaric acid —[ R05077, ]—> 4-hydroxy-4-methylglutamate  
EnergyScore: no! IndiScore: 60.2897

start\_Compound:pyruvate ||  
pyruvate —[ R00008, 4.1.3.17 ]—> 4-hydroxy-4-methyl-2-oxoglutaric acid —[ R05077, ]—> 4-hydroxy-4-methylglutamate  
EnergyScore: no! IndiScore: 60.2897

start\_Compound:D-citramalic acid ||  
D-citramalic acid —[ R03995, ]—> 4-hydroxy-4-methyl-2-oxoglutaric acid —[ R05077, ]—> 4-hydroxy-4-methylglutamate  
EnergyScore: no! IndiScore: 60.2897

start\_Compound:4-Methylene-2-oxoglutarate ||  
4-Methylene-2-oxoglutarate —[ R05078, 4.2.1.- ]—> 4-hydroxy-4-methyl-2-oxoglutaric acid —[ R05077, ]—> 4-hydroxy-4-methylglutamate  
EnergyScore: no! IndiScore: 60.2897

The results part displays all the Top pathways it found. Each pathway will be shown by the form of “compound 1-----[reaction 1, enzyme 1]---->compound 2”, and followed by EnergyScore (score calculated by Gibbs energy) and IndiScore (score calculated by the five features). Besides, the reverse pathway finder will output the start compound end with ‘||’ at the beginning of each result.

However, you may not know which one to choose. The EnergyScore is the first choice criteria, the lower which is, the better this pathway may be. Then, it would help if you considered the higher IndiScore. If you input a big ratio to any feature(KM, KKM, Toxicity, PH, Temperature), which means you value a particular condition, you should consider IndiScore first or consider both.

#### ● About debug

Our software is the 1.0 version, so there will be many bugs in it, although we have fixed some bugs. For more normal functions, this version may not fit the users. If you input an illogical compound or number, we popup a window to warn you and then return to the page and fill in the default values. Meanwhile, we will show you an example of the compound id. If you input a compound not found in our database, we will also warn, but you may need to try other compounds.

please input use number with type float!

确定

Sorry but Not Found the start compound asda ! please input like C00051.

确定

## Pathway Finder

### 1. Search form start compound to the target

input start and end compound

asda

sadasddd

set your weight of the pathway ranking, including KM(Michaelis constant), KKM(Kcat/Km), toxicity, PH and tempreature

0.2

0.2

0.2

0.2

0.2

Search

## Deep Metabolic Simulation

- About page

Click the navigation card on the home page or '/HMS' to enter the Deep Metabolic Simulation module.

Similar to the pathway finder page, the DMS search is put in the center of this page.

### DMS(Deep Metabolic Simulation)

Observation list: input the compounds you want to observe,using';'to separate

Delete reactions: input the reactions you want to delete,using';'to separate

default value: The default value of compounds

default epochs: The default number of run

The specified value of compounds:

input like C00001: 100000, C00002: 100000, C00003: 100000 using 'compound : value' as input

RUN DMS

In the search windows, there are some input parameters. The first one is observation\_list, which is the compound you want to observe, and we will show them in the top of the results with red color. Second one is delete\_reaction\_list. You can delete some reactions to block the paths between molecules. Default value is an initial default value of all the compounds; we will define the compounds'

[randomwalk\\_res\\_2020\\_10\\_24\\_2543771.pdf](#)

[randomwalk\\_res\\_2020\\_10\\_24\\_2543771.csv](#)

[Back to The Home Page](#)

amount with this number. Default\_epochs is the iteration times our algorithm will go through.

At last, the most critical parameter is specified\_values. You can define every specified compound with an initial value, and we will replace this compound's default value with it. When you input all the parameters, you can click the RUN DMS button to run the algorithm. You may need to wait for some minutes, and then you can get two results. One is a PDF file in which we show the compounds in observation\_list and whose value's change is in rank TOP50, another one is CSV file, we output all the change information of all compounds.

- About functions

DMS aims to provide simulations of metabolism in a computational environment. Our Metabolism Simulation tool's core is random walking, which is like the Monte-Carlo method, and the difference is that random walking is applied to a graph.

Users input the default value of common compounds and the specified values of particular compounds, which are hypothetical parameters referred to as the number of molecules or the molecular level. Then, we construct an environment (or graph) that contains all reactions and all molecules (compounds), giving these reactants initial states with the user-defined values; You can also eliminate some reaction (the reaction\_deficient\_list) according to the demand; these reactions may be which you want to block or have inhibited in gene level. Eliminated reactions will no longer provide the molecules' transformation on both sides of the reaction. Then we simulate the process of metabolic reactions, let these molecules randomly transform to others until it reaches an equilibrium state. Users can adjust the times of metabolic simulations through epochs. The larger the epochs, the more DMS functions iterate, and the more stable DMS results are. For users' convenience, we've provided an observation list for the compounds you want to observe (get the change of these compounds), and we're going to put them first on the top in PDF with red color.

- About results

We will show you two download links for our results. One is PDF divided into three parts: Summary, Results, and Annotation, and the other one is a CSV data file.

## RandomWalking

### Summary:

```
observation_compound(the compound you want to observe, which is label with color red!):  
C00797,C00008  
reaction_deficient:  
default_value: 100, epoches: 5000, thread: 8  
specified_value(the compound you altered, which is label with color red!):  
C00002: 500, C00008: 595, C00020: 955, C00003: 10, C00004: 100, C00006: 195, C00005: 62,  
C00010: 123, C00009: 100, C00011: 1350, C00014: 10000, C00031: 220000, C00095: 230000,  
C00092: 3480, C00085: 600, C00354: 272, C00118: 218, C00111: 167, C03339: 8, C00197: 2500,  
C00074: 2670, C00022: 2670, C04442: 808, C00199: 111, C01101: 111, C00117: 398, C00231:  
138, C03291: 138, C00279: 980, C05382: 276, C00024: 300, C00036: 680, C00158: 150, C00311:  
170, C00026: 180, C00042: 190, C00149: 60, C00497: 60, C00049: 1340, C00402: 1340, C00575:  
8, C00001: 1000,
```

You can find the initial state value in the summary part shown in default\_value and specified\_value. The specified values include some compound values in the experiment we get from the article and the values you input. In this condition, most compounds will begin with the default value, and the specified compounds will start at specified values (of course, the specified values you input have the highest priority).

The observation compounds are the compounds you want to observe, which is a label with the color red, and we put them on the TOP of results!

For a better experience, we show the TOP50 (now TOP100) of the compounds' normalize delta. Every result is output in "compound id: compounds name, final

#### Results(TOP50):

C00797: ethylamine, 97.875, delta:-2.125, normalize\_delta:-0.02125  
 C00008: ADP, 405.375, delta:-189.625, normalize\_delta:-0.3187  
 C00003: NAD(+), 110.75, delta:100.75, normalize\_delta:10.075  
 C00007: dioxygen, 945.0, delta:845.0, normalize\_delta:8.45  
 C00019: S-adenosyl-L-methionine, 238.5, delta:138.5, normalize\_delta:1.385  
 C00009: phosphate(3-), 0.0, delta:-100.0, normalize\_delta:1.0  
 C00013: diphosphate(4-), 0.0, delta:-100.0, normalize\_delta:1.0  
 C00015: UDP, 0.0, delta:-100.0, normalize\_delta:1.0  
 C03024: Reduced flavoprotein, 200.0, delta:100.0, normalize\_delta:1.0  
 C03161: Oxidized flavoprotein, 0.0, delta:-100.0, normalize\_delta:1.0  
 C00021: S-adenosyl-L-homocysteine, 0.125, delta:-99.875, normalize\_delta:0.99875  
 C00010: coenzyme A, 0.25, delta:-122.75, normalize\_delta:0.99797  
 C00004: NADH, 1.5, delta:-98.5, normalize\_delta:0.985  
 C00027: hydrogen peroxide, 9.25, delta:-90.75, normalize\_delta:0.9075  
 C00138: reduced ferredoxin, 189.625, delta:89.625, normalize\_delta:0.89625  
 C00139: oxidized ferredoxin, 10.375, delta:-89.625, normalize\_delta:0.89625  
 C00022: holo-[acyl-carrier protein], 80.5, delta:-19.5, normalize\_delta:0.195  
 C00060: monocarboxylic acid anion, 81.75, delta:-18.25, normalize\_delta:0.1825  
 C00043: UDP-N-acetyl-alpha-D-glucosamine, 117.0, delta:17.0, normalize\_delta:0.17  
 C00048: glyoxylic acid, 83.125, delta:-16.875, normalize\_delta:0.16875  
 C05359: electron, 116.125, delta:16.125, normalize\_delta:0.16125  
 C00028: acceptor, 115.875, delta:15.875, normalize\_delta:0.15875

state, change *delta*, normalized *delta*". Change *delta* is equal to final value minus initial value:  $delta = final\ value - initial\ value$ , and normalized *delta* is equal to change *delta* divided by the initial value:

$$normalized\ delta = \frac{\Delta value(delta)}{initial\ value}$$

#### Annotation:

we output the compound you want to observe, and the top50 compound which altered and ordered by alter number(delta), the output features are compound id, compound name, the Final state value, altered value and normalized altered value from left to right. if you want to get all results, please download the .csv file!

At the end of this PDF, we give you Annotation to find this handbook to know more details, and also you can download the CSV file for more analysis, in which we output all the compounds and their values.



compound	start_value	end_value	delta	normalize_delta
C00001	1000	873.25	-126.75	0.12675
C00002	500	730.75	230.75	0.4615
C00003	10	110.75	100.75	10.075
C00004	100	1.5	-98.5	0.985
C00005	62	85.625	23.625	0.38105
C00006	195	171.0	-24.0	0.12308
C00007	100	945.0	845.0	8.45
C00008	595	405.375	-189.625	0.3187
C00009	100	0.0	-100.0	1.0
C00010	123	0.25	-122.75	0.99797
C00011	1350	1017.625	-332.375	0.2462
C00012	100	98.75	-1.25	0.0125
C00013	100	0.0	-100.0	1.0
C00014	10000	9860.375	-139.625	0.01396
C00015	100	0.0	-100.0	1.0
C00016	100	108.0	8.0	0.08
C00017	100	104.375	4.375	0.04375
C00018	100	97.75	-2.25	0.0225
C00019	100	238.5	138.5	1.385
C00020	955	904.875	-50.125	0.05249
C00021	100	0.125	-99.875	0.99875
C00022	2670	2638.875	-31.125	0.01166
C00023	100	100.0	0.0	0.0

### ● About debug

Our software is the 1.0 version, so there will be many bugs in it, although we have fixed some bugs. For more normal functions, this version may not fit the user. If you input an illogical compound, reaction, or number, we will pop up a window to warn you and then return to the page and fill in the default values. Meanwhile, we will show you an example of the compound id or the reaction id. If you input a compound or reaction not in our database, we will also warn, but you may need to try another one.

Finally, if you input a text in an invalid format, for instance, you input a false separator but not the

Sorry but Not Found the compound C00075,C00322 ! please input like C00051!

确定

example we show you on the page, you will get a warning and modify the error until the function is running.

## DMS(Deep Metabolic Simulation)

Observation list: C00018;C00075,C00322

Delete reactions: input the reactions you want to delete,using';'to separate

default value: 100

default epochs: 500

The specified value of compounds:

C00002:4270,C00008:595,C00020:955,C00003:1470,C00004:100,C00006:195,C00005:62,C00010:123,C00009:

RUN DMS



## 4. Other pipelines

Our three modules are inter-related. Users can analyze the metabolic system with these modules and cooperate with other software to form a more standard pipeline. First, you can see the correlation between the reactants from DMS. In DMS, that changes of one molecule will result in other compounds' changes dramatically. Then you can go to Pathway Finder and search for the pathways between these two reactants. Second, users can search pathways between two compounds, and the reactions in these pathways can be deleted in DMS. as a result, you will find some unexpected results when you use DMS. Third, when you use other IGEM modules for project operation, such as eliminating a particular gene of one reaction or making part of the molecular level changes, you can input the changed level as the initial value into our DMS module, obtain more comprehensive molecules change within the metabolic system.

Meanwhile, you will find some alternative parameters to get more different results in our DMS code. You can choose better value or functions according to your demand. And we will give how to deploy:

Our software can be deployed on your own Linux server for a better performance. We have tested the deployment steps on CentOS 7.7.

### ### STEP I

Update your system and install docker.

```
>>curl -fsSL https://get.docker.com | bash -s docker --mirror Aliyun
```

### ### STEP II

Clone our repo and download extra data.

Put the downloaded files into the following directories.

```
>>mv ~/Download/db.sqlite3 Synthesis_Navigator-master/  
>>mv      ~/Download/Compound.csv      Synthesis_Navigator-  
master/statics/data_download/  
>>mv      ~/Download/Enzyme.csv      Synthesis_Navigator-  
master/statics/data_download/  
>>mv      ~/Download/Reaction.csv      Synthesis_Navigator-  
master/statics/data_download/  
>>mv      ~/Download/SyntheticBay.db      Synthesis_Navigator-  
master/statics/data_download/
```

### ### STEP III

Build docker image.

```
>>cd Synthesis_Navigator-master/  
>>docker build -t TongjiSoftware/Synthesis_Navigator:1.0 .
```

### ### STEP IV

Run the container.

```
>>docker run -it --rm -p 8000:8000 TongjiSoftware/Synthesis_Navigator:1.0
```

### ### STEP V

Open 127.0.0.1:8000/Home in your browser (Chrome is recommended).Enjoy:)  
You can modify settings.py to suit your environment.