Implementation correctness

Here we demonstrate the implementation correctness by comparing the result to exist implementation in R or C lang.

ORA and SPIA

The SPIA method including the result of ORA analysis thus we check the implementation of SPIA and ORA together in this section.

The result from R package SPIA

The code below could be found in SPIA's docs.

```
> library(SPIA)
> library(hgu133plus2.db)
> x <- hgu133plus2ENTREZID
> top$ENTREZ<-unlist(as.list(x[top$ID]))
> top<-top[!is.na(top$ENTREZ),]
> top<-top[!duplicated(top$ENTREZ),]
> tg1<-top[top$adj.P.Val<0.1,]
> DE_Colorectal=tg1$logFC
> names(DE_Colorectal)<-as.vector(tg1$ENTREZ)
> ALL_Colorectal=top$ENTREZ

>
res=spia(de=DE_Colorectal,all=ALL_Colorectal,organism="hsa",nB=2000,plots=FALSE,beta=NULL,combine="fish
```

And the top10 result is listed in the table below. (`Id` , `pSize` , `NDE` is removed for the space consideration)

	Name	pNDE	pPERT	pG	pGFdr	pGFWER	Status
0	Focal adhesion	1.009186e-07	0.000005	1.479215e-11	2.026525e-09	2.026525e-09	Activated
1	Alzheimer's disease	2.503714e-11	0.221000	1.489554e-10	1.020344e-08	2.040688e-08	Inhibited
2	ECM-receptor interaction	4.058570e-06	0.000005	5.199181e-10	2.374293e-08	7.122878e-08	Activated
3	Parkinson's disease	6.435720e-10	0.062000	9.953264e-10	3.408993e-08	1.363597e-07	Inhibited
4	Pathways in cancer	4.194045e-05	0.003000	2.124922e-06	5.822286e-05	2.911143e-04	Activated

The Result from PyPathway

```
from pypathway import *
c = ColorectalCancer()
r2 = SPIA.run(c.deg, c.background, organism="hsa")
```

The top5 result is list in the table below.

- the `seed` in the SPIA package can not be settled so in the result of `pG`, `pGfdr` and `pGFWER` there are some deviation but still in same order of magnitude。
- the result of `pNDE` indicate that the implementation of `ORA` is correct (In `PyPathway`, the `SPIA` and `ORA` use same implementation of `ORA`).

	name	pNDE	pPERT	pG	pGfdr	pGFWER	status
04510	Focal adhesion	1.00919e-07	5e-06	1.47922e-11	2.02653e-09	2.02653e-09	Activated
05010	Alzheimer's disease	2.50371e-11	0.232	1.56087e-10	1.0692e-08	2.1384e-08	Inhibited
04512	ECM-receptor interaction	4.05857e-06	5e-06	5.19918e-10	2.37429e-08	7.12288e-08	Activated
05012	Parkinson's disease	6.43572e-10	0.058	9.33601e-10	3.19758e-08	1.27903e-07	Inhibited
05200	Pathways in cancer	4.19405e-05	0.007	4.7094e-06	0.000129038	0.000645188	Activated

GSEA

We use the Java implementation from board institute to check the implementation correctness. The `class vector` and the `expression data` is available at Github. The GSEA algorithm, use random permutation to calculate NES and we can not use same random seed and random algorithm in `Java` and `Python`. So we compare the es of the top five pathway in KEGG enrichment and find that the result is identical to the original GSEA Java implementation

```
Term
Valine, leucine and isoleucine degradation_Homo sapiens_hsa00280   -0.836357
Glycerolipid metabolism_Homo sapiens_hsa00561                      -0.674108
Peroxisome_Homo sapiens_hsa04146                                   -0.672286
Fatty acid degradation_Homo sapiens_hsa00071                       -0.659410
Fatty acid metabolism_Homo sapiens_hsa01212                        -0.631014
Name: es, dtype: float64
```

Enrichnet

We use the we interface provided by `Enrichnet` to check the correctness of the method.

Result of the Enrichnet web interface

We perform the analysis with following parameters * Choose a molecular network: STRING * Identifier format: HGNC SYMBOL * gene identifier: we use the gene list derive from `ColorectalCancer` dataset

Derive

```
c = ColorectalCancer()
sym = IdMapping.convert(input_id=c.deg_list, source='ENTREZID', target="SYMBOL", species='hsa') sym =
[x[1][0] for x in sym if x[1]]
```

Result

	Annotation (pathway/process)	XD-score	Fisher q-value	Gene set size	Pathway size	Overlap size
0	hsa00280:Valine, leucine and isoleucine degrad...	4.334854	4.772740e-09	4342	44	35
1	hsa00603:Glycosphingolipid biosynthesis - glob...	3.895005	2.245753e-02	4342	14	10
2	hsa00640:Propanoate metabolism	3.673330	8.447069e-05	4342	32	23
3	hsa00410:beta-Alanine metabolism	3.316433	4.982290e-03	4342	22	15
4	hsa00900:Terpenoid backbone biosynthesis	3.252147	3.759063e-02	4342	15	10

Result of PyPathway

Code

```
c = ColorectalCancer()
# convert ENTREZID to SYMBOL
sym = IdMapping.convert(input_id=c.deg_list, source='ENTREZID', target="SYMBOL", species='hsa')
sym = [x[1][0] for x in sym if x[1]]
# start analysis
en = Enrichnet.run(genesets=sym, graph='string')
```

Result

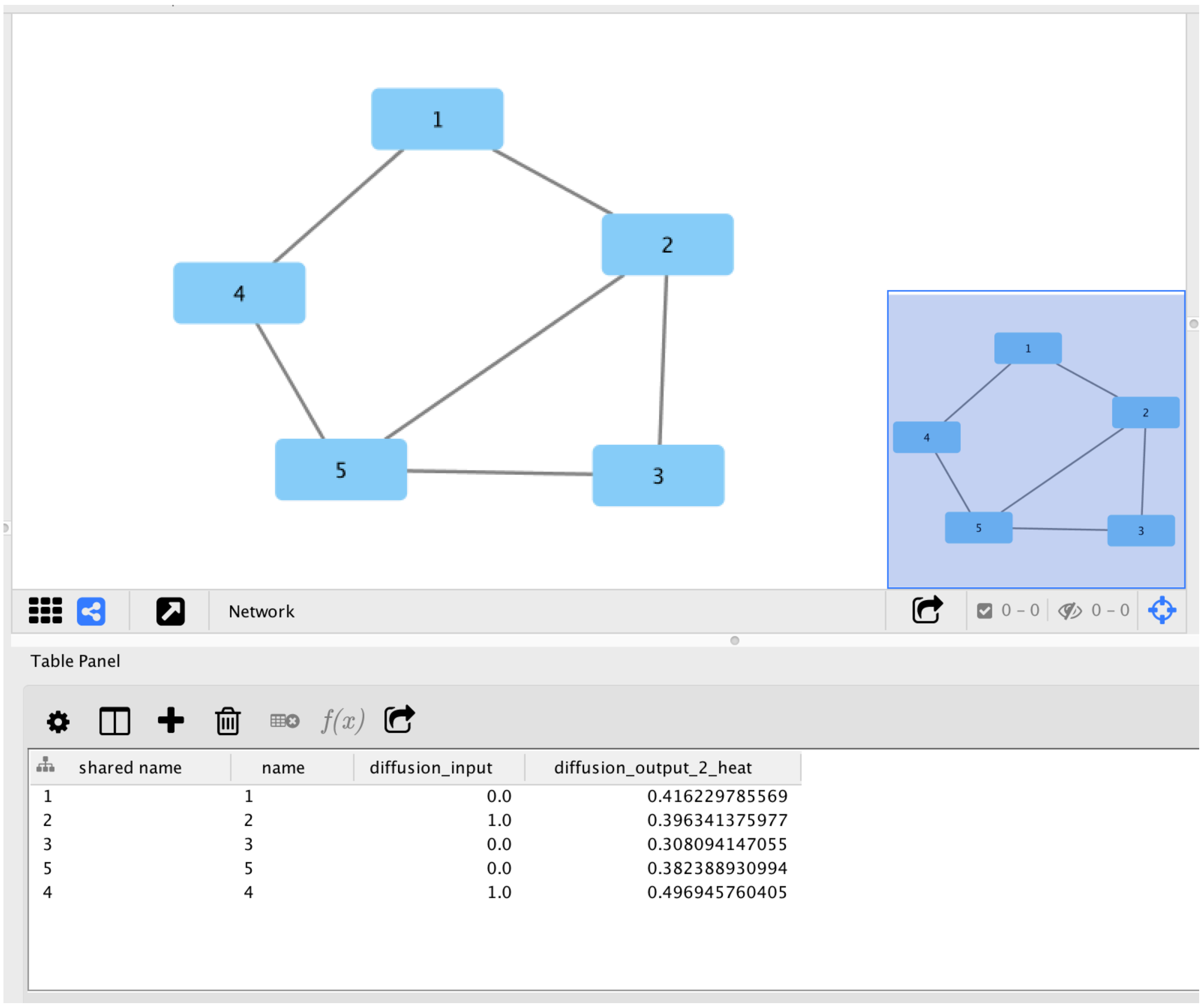
	Annotation (pathway/process)	XD-score	Fisher q-value	Gene set size	Pathway size	Overlap size
0	hsa00280:Valine, leucine and isoleucine degrad...	4.334854	4.772740e-09	4342	44	35
1	hsa00603:Glycosphingolipid biosynthesis - glob...	3.895005	2.245753e-02	4342	14	10
2	hsa00640:Propanoate metabolism	3.673330	8.447069e-05	4342	32	23
3	hsa00410:beta-Alanine metabolism	3.316433	4.982290e-03	4342	22	15
4	hsa00900:Terpenoid backbone biosynthesis	3.252147	3.759063e-02	4342	15	10

Network Propagation

Heat diffuse

We use Cytoscape Diffusion APP to check the correctness of the heat diffusion.

Result of Diffusion APP



shared name	name	diffusion_input	diffusion_output_2_heat
1	1	0.0	0.416229785569
2	2	1.0	0.396341375977
3	3	0.0	0.308094147055
5	5	0.0	0.382388930994
4	4	1.0	0.496945760405

Result of PyPathway

- code

```
from pypathway import diffusion_kernel
G = nx.Graph([[1, 2], [2, 3], [3, 5], [2, 5], [1, 4], [4, 5]])
h = np.array([0, 1, 0, 1, 0])
diffusion_kernel(G, h, rp=0.7, n=100).node
```

- result

```
{1: {'heat': 0.41720485133090102},
 2: {'heat': 0.39506307105908312},
 3: {'heat': 0.30896131580088793},
 4: {'heat': 0.49570801546580717},
 5: {'heat': 0.38306274634330961}}
```

MAGI

Pathway select

The test file of MAGI could be found in Github, and we use a modified C version of MAGI only set the random seed to 10 and compile it in `macOS 10.12.6` and compiler `LLVM 9.0` to generate a random free result.

original

- **pathway select**

```
./Pathway_Select -p StringNew_HPRD.txt -c ID_2_Autism_4_Severe_Missense.Clean_WithNew.txt -h
GeneCoExpresion_ID.txt -e adj1.csv.Tab.BinaryFormat -d New_ESP_Sereve.txt -l Gene_Name_Length.txt -i
0
```

- **cluster**

```
-c RandomGeneList.0 -a 0.3 -s seeds -avgCoExpr 0.415 -avgDensity 0.08 -e adj1.csv.Tab.BinaryFormat -l
5 -i cluster -p StringNew_HPRD.txt -h GeneCoExpresion_ID.txt -m 1 -u 10 -minCoExpr 0.01
```

PyPathway

- **pathway select**

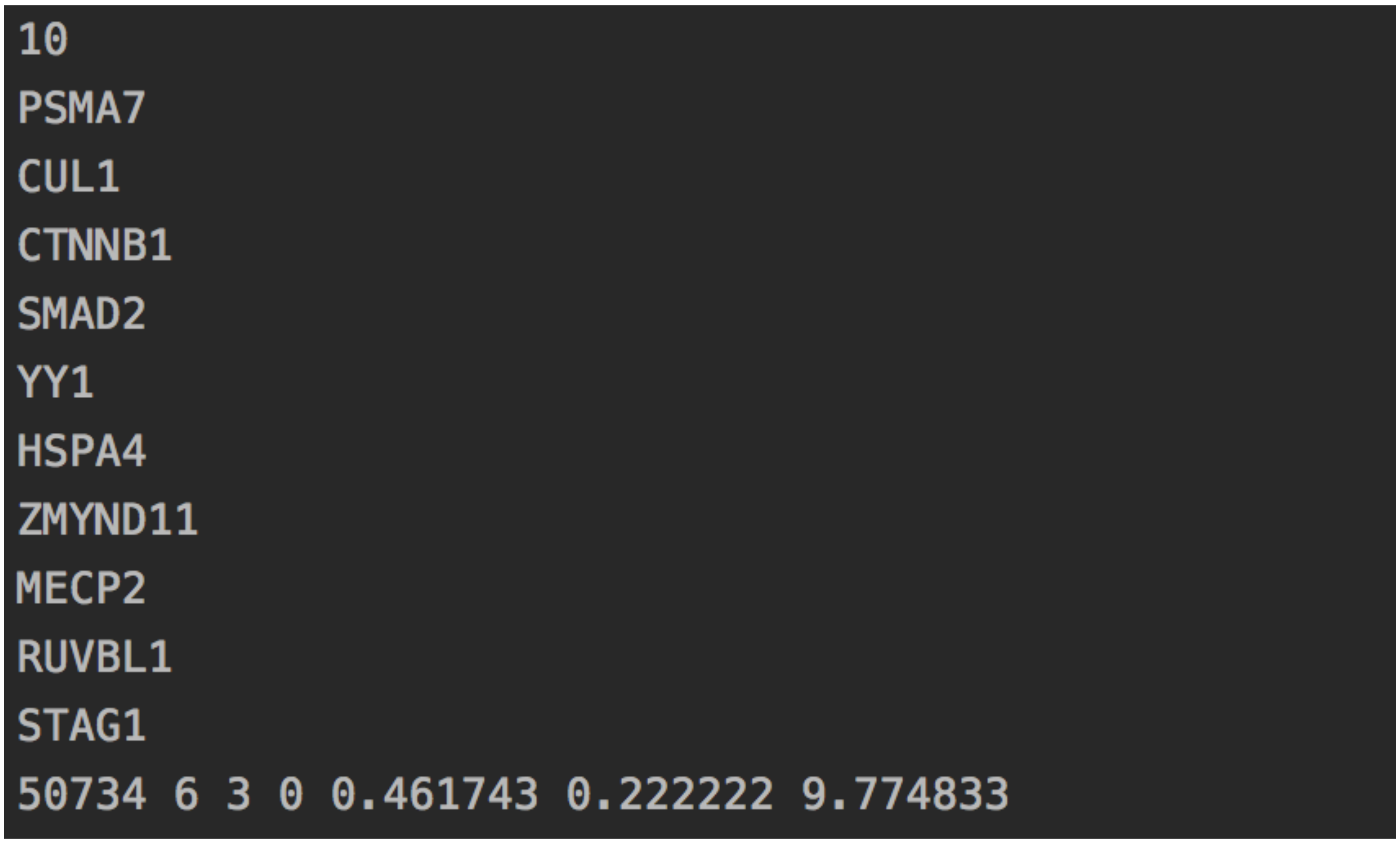
```
MAGI.select_pathway(
    path + 'StringNew_HPRD.txt',
    path + 'ID_2_Autism_4_Severe_Missense.Clean_WithNew.txt',
    path + 'GeneCoExpresion_ID.txt', path + 'adj1.csv.Tab.BinaryFormat',
    path + 'New_ESP_Sereve.txt',
    path + 'Gene_Name_Length.txt',
    rand_seed = 10
)
```

- **cluster**

```
r = MAGI.cluster(
    path + 'StringNew_HPRD.txt', path + 'GeneCoExpresion_ID.txt',
    path + 'adj1.csv.Tab.BinaryFormat', 10, 5, 10, 0.3
)
```

Result

In original version:



```
10
PSMA7
CUL1
CTNNB1
SMAD2
YY1
HSPA4
ZMYND11
MECP2
RUVBL1
STAG1
50734 6 3 0 0.461743 0.222222 9.774833
```

We get same highest scored submodule:

```
r[0].genes.keys()
```

```
dict_keys(['STAG1', 'MECP2', 'ZMYND11', 'CTNNB1', 'PSMA7', 'RUVBL1', 'YY1', 'SMAD2', 'HSPA4', 'CUL1'])
```