# MetaboSPAN-vignette

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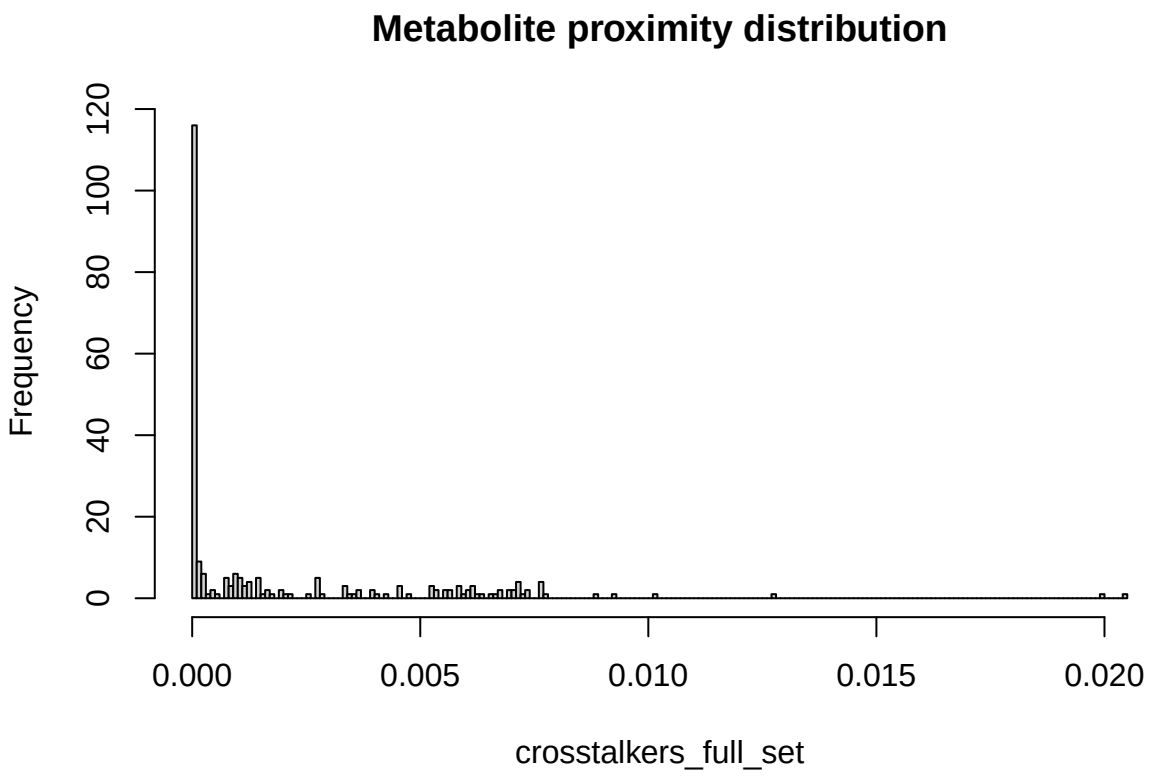
## Introduction

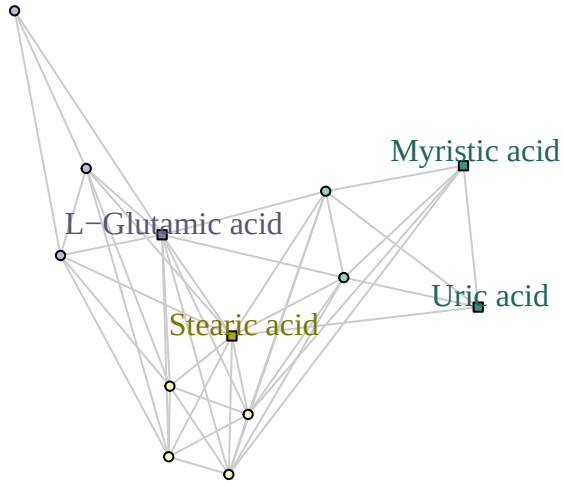
MetaboSPAN is being run on a pathway network based on RaMP2. Relevant stats about the analysis are listed in the table below.

```
library(metabospan)
library(RaMP)
library(magrittr)
library(dplyr)

conpass_bw = 'mysql123'
host_bw = "localhost"
dbname_bw = "ramp2"
username_bw = "root"
socket_bw=paste0(
    '/lscratch/',
    Sys.getenv('SLURM_JOB_ID'),
    '/mysql/mysql.sock')

## Parameters for MetaboSPAN
metabs_of_interest_cutoff=5
background_cutoff=5

load("../data/example_metabolites.rda")

start_time=Sys.time()
```

```
start=Sys.time()
metabolite_distances=measure_metabolite_distance(metabolites,
                                                 biospecimen = "Adipose",
                                                 conpass=conpass_bw,
                                                 socket=socket_bw, dbname=dbname_bw)
#> setting diag of graph to zero
#> Correcting for hub degrees.
#> normalizing column vectors!
#> normalizing column vectors!
print(Sys.time()-start)
#> Time difference of 0.03996062 secs

visualize_metabolite_distances(metabolite_distances)
abline(v=metabs_of_interest_cutoff)
```




```
proximal_metabolites<-extract_proximal_metabolites(
    metabolites,
    metabolite_distances,
    biospecimen = "Adipose",
    absolute_cutoff=metabs_of_interest_cutoff,
    conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw
)
#> [1] "Extracting 5 metabolite(s)"

visualize_metabolite_network(metabolites,
                             proximal_metabolites, biospecimen = "Adipose",
                             label=TRUE,
                             conpass=conpass_bw, socket=socket_bw, dbname=dbname_bw)
```



```
metabolite_panel<-c(background_ids,proximal_metabolites)
metabolite_panel<-metabolite_panel[which(!is.na(metabolite_panel))]

metabolite_distances_bg=measure_metabolite_distance(
    metabolite_panel,
    biospecimen = "Adipose",
    conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw)
#> setting diag of graph to zero
#> Correcting for hub degrees.
#> normalizing column vectors!
#> normalizing column vectors!

proximal_metabolites_bg<-extract_proximal_metabolites(
    metabolite_panel,
    metabolite_distances_bg,
    biospecimen = "Adipose",
    absolute_cutoff=background_cutoff,
    conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw
)
#> [1] "Extracting 5 metabolite(s)"


expanded_metabolites_of_interest=c(metabolites,
              as.vector(proximal_metabolites))

## Get pathways from RaMP
pathwaydf <-
    getPathwayFromAnalyte(
        analytes = expanded_metabolites_of_interest,
        NameOrIds="ids",
        conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw)

expanded_background = c(metabolite_panel,
          proximal_metabolites_bg)

backgrounddf <-getPathwayFromAnalyte(
    analytes = expanded_background,
    NameOrIds="ids",
    conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw)

pathways_FDR<-runCombinedFisherTest(pathwaydf,
                                    backgrounddf,
                                    biospecimen_background="Adipose",
                                    conpass=conpass_bw,socket=socket_bw,
                                    dbname = dbname_bw,
                                    MCall=F)
#> [1] "Running Fisher's tests on metabolites"
#> [1] "Fisher Testing ......"
#> [1] "Keeping 92 pathways"
#> [1] "Calculated p-values for 157 pathways"
#> [1] 92  4
#> [1] "pathwayRampId" "Pval"          "Num_In_Path"   "Total_In_Path"
```

```
## plot_pathway_results(pathways,thresh=0.1,title="MetaboSPAN results")
```

```
pathwaydf_default<-
    getPathwayFromAnalyte(
        analytes =
            c(metabolites),
        NameOrIds="ids",
        conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw)

backgrounddf_default <-getPathwayFromAnalyte(
    analytes =
        c(as.vector(background_ids)),
    NameOrIds="ids",
        conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw)

pathways_FDR_default<-
    runCombinedFisherTest(pathwaydf_default,
                          backgrounddf_default,
                          biospecimen_background = "Adipose",
                          MCall=F,
                          conpass=conpass_bw,socket=socket_bw, dbname=dbname_bw)
#> [1] "Running Fisher's tests on metabolites"
#> [1] "Fisher Testing ......"
#> [1] "Keeping 45 pathways"
#> [1] "Calculated p-values for 87 pathways"
#> [1] 45  4
#> [1] "pathwayRampId" "Pval"          "Num_In_Path"   "Total_In_Path"
```

# Pathway Results

## Pathways Summary table

| stat | value |
|---|---|
| Number of significant metabolites | 16.00 |
| Number of panel metabolites | 511.00 |
| Similarity cutoff for significant list addition | 5.00 |
| Similarity cutoff for background list addition | 5.00 |
| Number of metabolites added to significant list | 5.00 |
| Number of metabolites added to panel list | 5.00 |
| Number of MetaboSPAN pathways with FDR pval $< 0.05$ | 22.00 |
| Number of conventional (unexpanded) pathways with FDR pval $< 0.05$ | 4.00 |
| Number of MetaboSPAN pathways with nominal pval $< 0.05$ | 22.00 |
| Number of conventional (unexpanded) pathways with nominal pval $< 0.05$ | 4.00 |
| Jaccard overlap of pathways $< 0.05$ between methods | 1.00 |
| Time it took to generate this report (minutes) | 0.36 |

## Significant MetaboSPAN pathways ($p < 0.05$)

```
pathways_FDR$fishresults%>%dplyr::filter(Pval<0.05)%>%
    dplyr::select(pathwayName, Pval_FDR, Pval) %>%
    dplyr::arrange(pathwayName) %>%
```

```
    knitr::kable()
```

| pathwayName | Pval_FDR | Pval |
|---|---|---|
| Biogenic amine synthesis | 0.0000368 | 6.40e-06 |
| Class A/1 (rhodopsin-like receptors) | 0.0000010 | 1.00e-07 |
| Disorders of transmembrane transporters | 0.0001016 | 2.43e-05 |
| Free fatty acid receptors | 0.0000596 | 1.29e-05 |
| G alpha (q) signaling events | 0.0000006 | 1.00e-07 |
| G alpha (q) signalling events | 0.0000007 | 1.00e-07 |
| Incretin synthesis, secretion, and inactivation | 0.0000003 | 0.00e+00 |
| Incretin synthesis, secretion, and inactivation | 0.0000003 | 0.00e+00 |
| Methionine de novo and salvage pathway | 0.0000184 | 3.00e-06 |
| Neuronal System | 0.0000003 | 0.00e+00 |
| Neurotransmitter release cycle | 0.0000003 | 0.00e+00 |
| Neurotransmitter release cycle | 0.0000567 | 1.11e-05 |
| Omega-9 fatty acid synthesis | 0.0000000 | 0.00e+00 |
| Peptide hormone metabolism | 0.0000003 | 0.00e+00 |
| Phosphatidylcholine catabolism | 0.0000002 | 0.00e+00 |
| Purine metabolism and related disorders | 0.0000184 | 3.00e-06 |
| SLC transporter disorders | 0.0000953 | 2.18e-05 |
| Synthesis, secretion, and inactivation of Glucagon-like Peptide-1 (GLP-1) | 0.0000003 | 0.00e+00 |
| Trans-sulfuration and one-carbon metabolism | 0.0000101 | 1.40e-06 |
| Transmission across Chemical Synapses | 0.0000003 | 0.00e+00 |
| Transport of bile salts and organic acids, metal ions and amine compounds | 0.0000596 | 1.29e-05 |
| Transport of bile salts and organic acids, metal ions and amine compounds | 0.0000567 | 1.11e-05 |

## Significant default pathways ($p < 0.05$)

```
pathways_FDR_default$fishresults%>%dplyr::filter(Pval<0.05) %>%
    dplyr::select(pathwayName, Pval_FDR, Pval) %>%
    dplyr::arrange(pathwayName) %>%
    knitr::kable()
```

| pathwayName | Pval_FDR | Pval |
|---|---|---|
| Disorders of transmembrane transporters | 4.57e-05 | 4.1e-06 |
| Omega-9 fatty acid synthesis | 1.50e-05 | 7.0e-07 |
| Purine metabolism and related disorders | 1.50e-05 | 5.0e-07 |
| SLC transporter disorders | 4.57e-05 | 3.6e-06 |

## Metabolites added to set of interest

```
if(length(proximal_metabolites)!=0){
    knitr::kable(metabospan:::source_to_common(proximal_metabolites,
                                               conpass=conpass_bw,
                                               socket=socket_bw, dbname=dbname_bw))
}
```

| | commonName |
|---|---|
| 1 | Betaine |
| 3 | L-Carnitine |

| | commonName |
|---|---|
| 4 | Palmitelaidic acid |
| 6 | Acetylcholine |
| 8 | Stearoyl-CoA |

### Metabolites added to background

```
if(length(proximal_metabolites_bg)!=0){
    knitr::kable(metabospan:::source_to_common(proximal_metabolites_bg,
                                               conpass=conpass_bw,
                                               socket=socket_bw, dbname=dbname_bw))
}
```

| | commonName |
|---|---|
| 1 | Prostaglandin D2 |
| 4 | Epinephrine |
| 6 | Oleic acid |
| 9 | Nicotinic acid |
| 11 | TG(16:0/18:0/18:2(9Z,12Z)) |

## Chemical