

# main

October 1, 2021

## 1 Exploring the eigen values and correlation with phenotypes

```
[1]: suppressPackageStartupMessages({  
      library(ComplexHeatmap)  
      library(tidyverse)  
      library(ggpubr)  
    })
```

### 1.1 Prepare data

#### 1.1.1 Load phenotypes data

```
[2]: pheno = data.table::fread("../.../input/phenotypes/merged/_m/  
      ↪merged_phenotypes.csv")  
pheno %>% head(2)
```

	V1	BrNum	RNum	Region	RIN	Age	Sex	Race	Dx	mito
	<chr>	<chr>	<chr>	<chr>	<dbl>	<dbl>	<chr>	<chr>	<chr>	<dbl>
A data.table: 2 × 12	R12864	Br1303	R12864	Caudate	9.6	42.98	F	AA	Schizo	0.032
	R12865	Br1320	R12865	Caudate	9.5	53.12	M	AA	Schizo	0.019

```
[3]: ancestry = data.table::fread("../.../input/ancestry_structure/structure.  
      ↪out_ancestry_proportion_raceDemo_compare")  
ancestry %>% head(2)
```

	id	Afr	Eur	group
	<chr>	<dbl>	<dbl>	<chr>
A data.table: 2 × 4	Br2374	0.007	0.993	CAUC
	Br1857	0.001	0.999	CAUC

#### 1.1.2 Load eigen values

```
[4]: eigen = data.table::fread("../.../_m/eigengenes.csv")  
modules = eigen %>% select(-V1) %>% colnames  
eigen %>% dim  
eigen[1:2, 1:5]
```

1. 87 2. 40

	V1	MEblack	MEblue	MEbrown	MEcyan
A data.table: 2 × 5	<chr>	<dbl>	<dbl>	<dbl>	<dbl>
	R10700	-0.02635168	-0.03415886	-0.02078395	0.05489625
	R10706	-0.06053349	-0.07077148	-0.03261367	0.07795030

### 1.1.3 Merge data

```
[5]: dt = eigen %>% left_join(pheno, by="V1") %>%
      inner_join(ancestry, by=c("BrNum"="id"))
      dt %>% dim
      dt[1:2, 1:5]
```

1. 87 2. 54

	V1	MEblack	MEblue	MEbrown	MEcyan
A data.table: 2 × 5	<chr>	<dbl>	<dbl>	<dbl>	<dbl>
	R10700	-0.02635168	-0.03415886	-0.02078395	0.05489625
	R10706	-0.06053349	-0.07077148	-0.03261367	0.07795030

## 1.2 Examine correlation of modules with ancestry

### 1.2.1 Linear model

```
[6]: pvals = c()
      for(mod in modules){
        model = paste0("Eur ~ ", mod)
        res = anova(lm(model, data=dt))
        pvals = c(pvals, res[mod, "Pr(>F)"])
      }
      fdr <- p.adjust(pvals, method="fdr")
      df1 = data.frame("Modules"=modules, "Pvalue"=pvals, "FDR"=fdr)
      df1 %>% filter(FDR < 0.05)
```

	Modules	Pvalue	FDR
A data.frame: 8 × 3	<chr>	<dbl>	<dbl>
	MEblack	7.602563e-03	4.966458e-02
	MEdarkgrey	7.190295e-04	9.347383e-03
	MEdarkolivegreen	1.664925e-03	1.623302e-02
	MEgrey	9.032128e-06	1.761265e-04
	MEgrey60	4.711608e-08	1.837527e-06
	MElightcyan	9.443591e-03	4.966458e-02
	MEmagenta	7.749418e-03	4.966458e-02
	MEskyblue	1.018761e-02	4.966458e-02

```
[7]: df1 %>% mutate(Tissue="Dentate Gyrus") %>%
      data.table::fwrite("eigen_correlation_ancestry.tsv", sep='\t')
```

### 1.2.2 Pearson correlation

```
[8]: pvals = c(); est = c()
for(mod in modules){
  res = cor.test(dt[["Eur"]], dt[[mod]], method="pearson")
  pvals = c(pvals, res$p.value)
  est = c(est, res$estimate[[1]])
}
fdr <- p.adjust(pvals, method="fdr")
df2 = data.frame("Modules"=modules, "Rho"=est, "Pvalue"=pvals, "FDR"=fdr)
df2 %>% filter(FDR < 0.05)
```

	Modules <chr>	Rho <dbl>	Pvalue <dbl>	FDR <dbl>
A data.frame: 8 × 4	MEblack	0.2843511	7.602563e-03	4.966458e-02
	MEdarkgrey	-0.3558145	7.190295e-04	9.347383e-03
	MEdarkolivegreen	0.3322760	1.664925e-03	1.623302e-02
	MEgrey	-0.4560540	9.032128e-06	1.761265e-04
	MEgrey60	0.5453477	4.711608e-08	1.837527e-06
	MElightcyan	0.2768170	9.443591e-03	4.966458e-02
	MEmagenta	-0.2836943	7.749418e-03	4.966458e-02
	MEskyblue	0.2741344	1.018761e-02	4.966458e-02

## 1.3 Clustering modules

### 1.3.1 Eigengene clustering

```
[9]: set.seed(13)
mat = eigen %>% column_to_rownames("V1") %>% as.matrix
pdf("eigengene_heatmap.pdf", width=10, height=8)
Heatmap(mat, name="Eigengene", column_dend_height=unit(3, "cm"),
  show_row_names=FALSE, show_row_dend=FALSE, column_km=4)
dev.off()
```

png: 2

### 1.3.2 clustering within significant module violet

```
[10]: load("../_m/01.RData", verbose=TRUE)
biomart_file = "../input/biomart/biomart.csv"
biomart = data.table::fread(biomart_file)
```

Loading objects:

```
datExpr
sample_table
datTraits
```

```
[11]: get_module_mat <- function(mod){
  MEmodule = data.table::fread("../_m/modules.csv", header=TRUE) %>%
```

```

    filter(module == mod)
mat0 = datExpr %>% as.data.frame %>%
  select(any_of(MEmodule$V1)) %>% as.matrix
annot = data.frame("Geneid"=colnames(mat0),
  "ensembl_gene_id"=gsub("\\..*", "", colnames(mat0))) %>%
  left_join(biomart, by="ensembl_gene_id") %>%
  distinct(ensembl_gene_id, .keep_all=TRUE) %>%
  mutate(external_gene_name=coalesce(external_gene_name,ensembl_gene_id))
#annot$external_gene_name %>% is.na %>% sum
colnames(mat0) <- annot$external_gene_name
return(mat0)
}

plot_module_heatmap <- function(mod, w, h){
  pdf(paste0(mod,"_module_heatmap.pdf"), width=w, height=h)
  set.seed(13)
  row_ha = rowAnnotation(EA = dt$Eur, AA = dt$Afr)
  ht = Heatmap(get_module_mat(mod),
    name="Residualized\nExpression",
    column_dend_height=unit(1, "cm"), row_km=2,
    show_row_names=FALSE, show_row_dend=TRUE,
    row_dend_width=unit(2, "cm"),
    right_annotation = row_ha)
  draw(ht)
  dev.off()
}

```

[12]: df1 %>% filter(FDR < 0.05)

	Modules <chr>	Pvalue <dbl>	FDR <dbl>
	MEblack	7.602563e-03	4.966458e-02
	MEdarkgrey	7.190295e-04	9.347383e-03
	MEdarkolivegreen	1.664925e-03	1.623302e-02
	MEgrey	9.032128e-06	1.761265e-04
	MEgrey60	4.711608e-08	1.837527e-06
	MElightcyan	9.443591e-03	4.966458e-02
	MEmagenta	7.749418e-03	4.966458e-02
	MEskyblue	1.018761e-02	4.966458e-02

A data.frame: 8 × 3

[13]: plot\_module\_heatmap("black", 24, 8)  
 plot\_module\_heatmap("darkgrey", 16, 8)  
 plot\_module\_heatmap("darkolivegreen", 12, 8)  
 plot\_module\_heatmap("grey60", 20, 8)  
 plot\_module\_heatmap("lightcyan", 20, 8)  
 plot\_module\_heatmap("magenta", 20, 8)  
 plot\_module\_heatmap("skyblue", 14, 8)

png: 2

png: 2

png: 2

png: 2

png: 2

png: 2

png: 2

```
[14]: plot_module_heatmap("grey", 20, 8)
```

The automatically generated colors map from the minus and plus 99<sup>th</sup> of the absolute values in the matrix. There are outliers in the matrix whose patterns might be hidden by this color mapping. You can manually set the color to ``col`` argument.

Use ``suppressMessages()`` to turn off this message.

``use_raster`` is automatically set to TRUE for a matrix with more than 2000 columns. You can control ``use_raster`` argument by explicitly setting TRUE/FALSE to it.

Set ``ht_opt$message = FALSE`` to turn off this message.

'magick' package is suggested to install to give better rasterization.

Set ``ht_opt$message = FALSE`` to turn off this message.

png: 2

## 1.4 Reproducibility Information

```
[15]: Sys.time()
      proc.time()
      options(width = 120)
      sessioninfo::session_info()
```

```
[1] "2021-10-01 13:35:41 EDT"
```

```
   user  system elapsed
60.478   2.514   63.595
```

```
Session info
```

```
setting  value
```

```
version  R version 4.0.3 (2020-10-10)
```

```
os       Arch Linux
```

```
system   x86_64, linux-gnu
```

```

ui          X11
language    (EN)
collate     en_US.UTF-8
ctype       en_US.UTF-8
tz          America/New_York
date        2021-10-01

```

#### Packages

package	* version	date	lib	source
abind	1.4-5	2016-07-21	[1]	CRAN (R 4.0.2)
assertthat	0.2.1	2019-03-21	[1]	CRAN (R 4.0.2)
backports	1.2.1	2020-12-09	[1]	CRAN (R 4.0.2)
base64enc	0.1-3	2015-07-28	[1]	CRAN (R 4.0.2)
BiocGenerics	0.36.1	2021-04-16	[1]	Bioconductor
broom	0.7.9	2021-07-27	[1]	CRAN (R 4.0.3)
Cairo	1.5-12.2	2020-07-07	[1]	CRAN (R 4.0.2)
car	3.0-11	2021-06-27	[1]	CRAN (R 4.0.3)
carData	3.0-4	2020-05-22	[1]	CRAN (R 4.0.2)
cellranger	1.1.0	2016-07-27	[1]	CRAN (R 4.0.2)
circlize	0.4.13	2021-06-09	[1]	CRAN (R 4.0.3)
cli	3.0.1	2021-07-17	[1]	CRAN (R 4.0.3)
clue	0.3-59	2021-04-16	[1]	CRAN (R 4.0.3)
cluster	2.1.0	2019-06-19	[2]	CRAN (R 4.0.3)
colorspace	2.0-2	2021-06-24	[1]	CRAN (R 4.0.3)
ComplexHeatmap	* 2.6.2	2020-11-12	[1]	Bioconductor
crayon	1.4.1	2021-02-08	[1]	CRAN (R 4.0.3)
curl	4.3.2	2021-06-23	[1]	CRAN (R 4.0.3)
data.table	1.14.2	2021-09-27	[1]	CRAN (R 4.0.3)
DBI	1.1.1	2021-01-15	[1]	CRAN (R 4.0.2)
dbplyr	2.1.1	2021-04-06	[1]	CRAN (R 4.0.3)
digest	0.6.28	2021-09-23	[1]	CRAN (R 4.0.3)
dplyr	* 1.0.7	2021-06-18	[1]	CRAN (R 4.0.3)
ellipsis	0.3.2	2021-04-29	[1]	CRAN (R 4.0.3)
evaluate	0.14	2019-05-28	[1]	CRAN (R 4.0.2)
fansi	0.5.0	2021-05-25	[1]	CRAN (R 4.0.3)
fastmap	1.1.0	2021-01-25	[1]	CRAN (R 4.0.2)
forcats	* 0.5.1	2021-01-27	[1]	CRAN (R 4.0.2)
foreign	0.8-80	2020-05-24	[2]	CRAN (R 4.0.3)
fs	1.5.0	2020-07-31	[1]	CRAN (R 4.0.2)
generics	0.1.0	2020-10-31	[1]	CRAN (R 4.0.2)
GetoptLong	1.0.5	2020-12-15	[1]	CRAN (R 4.0.2)
ggplot2	* 3.3.5	2021-06-25	[1]	CRAN (R 4.0.3)
ggpubr	* 0.4.0	2020-06-27	[1]	CRAN (R 4.0.2)
ggsignif	0.6.3	2021-09-09	[1]	CRAN (R 4.0.3)
GlobalOptions	0.1.2	2020-06-10	[1]	CRAN (R 4.0.2)
glue	1.4.2	2020-08-27	[1]	CRAN (R 4.0.2)
gtable	0.3.0	2019-03-25	[1]	CRAN (R 4.0.2)
haven	2.4.3	2021-08-04	[1]	CRAN (R 4.0.3)

hms	1.1.1	2021-09-26	[1]	CRAN	(R 4.0.3)
htmltools	0.5.2	2021-08-25	[1]	CRAN	(R 4.0.3)
httr	1.4.2	2020-07-20	[1]	CRAN	(R 4.0.2)
IRanges	2.24.1	2020-12-12	[1]	Bioconductor	
IRdisplay	1.0	2021-01-20	[1]	CRAN	(R 4.0.2)
IRkernel	1.2	2021-05-11	[1]	CRAN	(R 4.0.3)
jsonlite	1.7.2	2020-12-09	[1]	CRAN	(R 4.0.2)
lifecycle	1.0.1	2021-09-24	[1]	CRAN	(R 4.0.3)
lubridate	1.7.10	2021-02-26	[1]	CRAN	(R 4.0.3)
magrittr	2.0.1	2020-11-17	[1]	CRAN	(R 4.0.2)
matrixStats	0.61.0	2021-09-17	[1]	CRAN	(R 4.0.3)
modelr	0.1.8	2020-05-19	[1]	CRAN	(R 4.0.2)
munsell	0.5.0	2018-06-12	[1]	CRAN	(R 4.0.2)
openxlsx	4.2.4	2021-06-16	[1]	CRAN	(R 4.0.3)
pbdZMQ	0.3-5	2021-02-10	[1]	CRAN	(R 4.0.3)
pillar	1.6.3	2021-09-26	[1]	CRAN	(R 4.0.3)
pkgconfig	2.0.3	2019-09-22	[1]	CRAN	(R 4.0.2)
png	0.1-7	2013-12-03	[1]	CRAN	(R 4.0.2)
purrr	* 0.3.4	2020-04-17	[1]	CRAN	(R 4.0.2)
R6	2.5.1	2021-08-19	[1]	CRAN	(R 4.0.3)
RColorBrewer	1.1-2	2014-12-07	[1]	CRAN	(R 4.0.2)
Rcpp	1.0.7	2021-07-07	[1]	CRAN	(R 4.0.3)
readr	* 2.0.2	2021-09-27	[1]	CRAN	(R 4.0.3)
readxl	1.3.1	2019-03-13	[1]	CRAN	(R 4.0.2)
repr	1.1.3	2021-01-21	[1]	CRAN	(R 4.0.2)
reprex	2.0.1	2021-08-05	[1]	CRAN	(R 4.0.3)
rio	0.5.27	2021-06-21	[1]	CRAN	(R 4.0.3)
rjson	0.2.20	2018-06-08	[1]	CRAN	(R 4.0.2)
rlang	0.4.11	2021-04-30	[1]	CRAN	(R 4.0.3)
rstatix	0.7.0	2021-02-13	[1]	CRAN	(R 4.0.3)
rstudioapi	0.13	2020-11-12	[1]	CRAN	(R 4.0.2)
rvest	1.0.1	2021-07-26	[1]	CRAN	(R 4.0.3)
S4Vectors	0.28.1	2020-12-09	[1]	Bioconductor	
scales	1.1.1	2020-05-11	[1]	CRAN	(R 4.0.2)
sessioninfo	1.1.1	2018-11-05	[1]	CRAN	(R 4.0.2)
shape	1.4.6	2021-05-19	[1]	CRAN	(R 4.0.3)
stringi	1.7.4	2021-08-25	[1]	CRAN	(R 4.0.3)
stringr	* 1.4.0	2019-02-10	[1]	CRAN	(R 4.0.2)
tibble	* 3.1.4	2021-08-25	[1]	CRAN	(R 4.0.3)
tidyr	* 1.1.4	2021-09-27	[1]	CRAN	(R 4.0.3)
tidyselect	1.1.1	2021-04-30	[1]	CRAN	(R 4.0.3)
tidyverse	* 1.3.1	2021-04-15	[1]	CRAN	(R 4.0.3)
tzdb	0.1.2	2021-07-20	[1]	CRAN	(R 4.0.3)
utf8	1.2.2	2021-07-24	[1]	CRAN	(R 4.0.3)
uuid	0.1-4	2020-02-26	[1]	CRAN	(R 4.0.2)
vctrs	0.3.8	2021-04-29	[1]	CRAN	(R 4.0.3)
withr	2.4.2	2021-04-18	[1]	CRAN	(R 4.0.3)
xml2	1.3.2	2020-04-23	[1]	CRAN	(R 4.0.2)

```
zip                2.2.0    2021-05-31 [1] CRAN (R 4.0.3)

[1] /home/jbenja13/R/x86_64-pc-linux-gnu-library/4.0
[2] /usr/lib/R/library
```