Enrichment Analyses

Setup

```r
library(easypackages)
libraries("here")
options(stringsAsFactors = FALSE)

ndigits2use = 4

source(here("code","genelistOverlap.R"))
fdr_thresh = 0.05

# non-zero and zero modules
nmods = 21
nonzeromods = c(1,2,6,8,10,11,13,15,17,18,21)
zeromods = c(3,4,5,7,9,12,14,16,19,20)

# Load in gene lists for enrichment analyses
load(here("data","tidy","enrichment_data.Rdata"))
```

Read in data

```r
# read in WGCNA results
wgcna_res = read.csv(here("WGCNAresults","wgcna_results_summary.csv"))
backgroundTotal = dim(wgcna_res)[1]
bglist = wgcna_res$geneSymbol
M0_size = dim(subset(wgcna_res, wgcna_res$moduleLabels==0))[1]
```

Non-zero modules

Grab non-zero modules and report percentage of genes falling within those modules

```r
mask = is.element(wgcna_res$moduleLabels, nonzeromods)
nonzeromod_data = subset(wgcna_res, mask)
nz_genes = nonzeromod_data$geneSymbol
# percentage of clustered genes falling within those modules
nz_prop = dim(nonzeromod_data)[1]/(backgroundTotal-M0_size)
nz_prop
```

```
## [1] 0.6139912
```

Zero modules

Grab zero modules and report percentage of genes falling within those modules

```r
mask = is.element(wgcna_res$moduleLabels, zeromods)
zeromod_data = subset(wgcna_res, mask)
z_genes = zeromod_data$geneSymbol
```

```
# percentage of clustered genes falling within those modules
z_prop = dim(zeromod_data)[1]/(backgroundTotal-M0_size)
z_prop
```

```
## [1] 0.3860088
```

Annotate each module by enrichment in broadly expressed, blood, brain, or lymphocyte genes

```
mod_names = c("M1_turquoise","M2_blue","M3_brown","M4_yellow",
  "M5_green","M6_red","M7_black","M8_pink","M9_magenta",
  "M10_purple","M11_greenyellow","M12_tan","M13_salmon",
  "M14_cyan","M15_midnightblue","M16_lightcyan","M17_grey60",
  "M18_lightgreen","M19_lightyellow","M20_royalblue","M21_darkred")

geneclasses = c("BroadGenes","BloodGenes","BrainGenes","LymphocyteGenes")
outcols = c("OR","pval","fdr")

out_mats = vector(mode = "list", length = length(geneclasses))
names(out_mats) = geneclasses
for (igc in 1:length(geneclasses)){
  out_res = data.frame(matrix(nrow = length(mod_names),
                              ncol = length(outcols)))
  colnames(out_res) = outcols
  rownames(out_res) = mod_names

  # intersect genes2 list with background
  genes2 = eval(as.name(geneclasses[igc]))
  mask = is.element(genes2,bglist)
  genes2 = data.frame(genes2[mask])

  for (imod in 1:length(mod_names)){
    # filename for module list
    genes1 = wgcna_res$geneSymbol[wgcna_res$moduleLabels==imod]

    overlap_res = genelistOverlap(genes1,
                                  genes2,
                                  backgroundTotal,
                                  print_result = FALSE,
                                  header = FALSE)
    out_res[imod,1] = overlap_res[[1]]$OR
    out_res[imod,2] = overlap_res[[1]]$hypergeo_p
  }
  out_res[,3] = p.adjust(out_res[,2], method = "fdr")
  out_mats[[igc]] = out_res
}
```

Modules enriched for broadly expressed genes

```
out_mats[[1]]
```

```
##                         OR         pval          fdr
## M1_turquoise     1.4754869 7.384191e-05 2.215257e-04
## M2_blue          4.3473823 2.843457e-59 5.971260e-58
## M3_brown         0.4028520 1.000000e+00 1.000000e+00
## M4_yellow        1.0127503 5.891632e-01 1.000000e+00
## M5_green         0.8250661 9.591967e-01 1.000000e+00
## M6_red           0.6841978 9.982855e-01 1.000000e+00
## M7_black         0.6557372 9.990008e-01 1.000000e+00
## M8_pink          3.4594286 5.151937e-23 5.409534e-22
## M9_magenta       0.9673481 6.687839e-01 1.000000e+00
## M10_purple       1.7558107 6.361290e-05 2.215257e-04
## M11_greenyellow  2.8354308 5.456839e-14 2.864840e-13
## M12_tan          0.9602873 6.756651e-01 1.000000e+00
## M13_salmon       3.2416943 6.186578e-17 4.330604e-16
## M14_cyan         0.8460565 8.385310e-01 1.000000e+00
## M15_midnightblue 2.9259899 8.821725e-10 3.705125e-09
## M16_lightcyan    0.2184977 1.000000e+00 1.000000e+00
## M17_grey60       0.3078006 9.999977e-01 1.000000e+00
## M18_lightgreen   2.0544133 1.640082e-04 4.305215e-04
## M19_lightyellow  0.1180096 1.000000e+00 1.000000e+00
## M20_royalblue    0.8797679 7.608833e-01 1.000000e+00
## M21_darkred      1.8493827 2.375546e-03 5.542940e-03
```

Modules enriched for whole-blood-specific genes

```
out_mats[[2]]
```

```
##                          OR         pval          fdr
## M1_turquoise     11.5273292 4.658437e-56 9.782719e-55
## M2_blue           0.0000000 1.000000e+00 1.000000e+00
## M3_brown          0.4055741 9.808647e-01 1.000000e+00
## M4_yellow         0.0000000 1.000000e+00 1.000000e+00
## M5_green          0.0000000 1.000000e+00 1.000000e+00
## M6_red            0.0000000 1.000000e+00 1.000000e+00
## M7_black          4.7788779 8.944644e-08 9.391876e-07
## M8_pink           0.0000000 1.000000e+00 1.000000e+00
## M9_magenta        2.1295290 4.617022e-02 1.615958e-01
## M10_purple        0.0000000 1.000000e+00 1.000000e+00
## M11_greenyellow   0.2711242 9.758859e-01 1.000000e+00
## M12_tan           2.3397400 2.934126e-02 1.232333e-01
## M13_salmon        0.8751862 6.778683e-01 1.000000e+00
## M14_cyan          0.4169821 9.110777e-01 1.000000e+00
## M15_midnightblue  0.0000000 1.000000e+00 1.000000e+00
## M16_lightcyan     5.8975148 8.474162e-06 5.931914e-05
## M17_grey60        0.0000000 1.000000e+00 1.000000e+00
## M18_lightgreen    0.0000000 1.000000e+00 1.000000e+00
## M19_lightyellow   5.9327166 2.006122e-05 1.053214e-04
## M20_royalblue     0.0000000 1.000000e+00 1.000000e+00
```

```
## M21_darkred        0.0000000 1.000000e+00 1.000000e+00
```

Modules enriched for brain-specific genes

```
out_mats[[3]]
```

```
##                          OR        pval        fdr
## M1_turquoise      0.6372773 0.993733802 1.00000000
## M2_blue           0.1048834 0.999939871 1.00000000
## M3_brown          0.9104730 0.682859810 1.00000000
## M4_yellow         0.3257368 0.985882512 1.00000000
## M5_green          0.8687475 0.702908371 1.00000000
## M6_red            0.7366275 0.804434834 1.00000000
## M7_black          2.7368728 0.002137245 0.04488215
## M8_pink           0.0000000 1.000000000 1.00000000
## M9_magenta        0.2348909 0.986403449 1.00000000
## M10_purple        0.0000000 1.000000000 1.00000000
## M11_greenyellow   0.2542235 0.981117101 1.00000000
## M12_tan           1.0567651 0.540726528 1.00000000
## M13_salmon        0.0000000 1.000000000 1.00000000
## M14_cyan          0.7904823 0.725793834 1.00000000
## M15_midnightblue  0.0000000 1.000000000 1.00000000
## M16_lightcyan     1.3649312 0.388779322 1.00000000
## M17_grey60        0.4444339 0.896601020 1.00000000
## M18_lightgreen    0.0000000 1.000000000 1.00000000
## M19_lightyellow   2.5990629 0.051837402 0.54429272
## M20_royalblue     0.0000000 1.000000000 1.00000000
## M21_darkred       0.5515742 0.839551585 1.00000000
```

Modules enriched for lymphocyte-specific genes

```
out_mats[[4]]
```

```
##                           OR         pval          fdr
## M1_turquoise       0.1838656 1.000000e+00 1.000000e+00
## M2_blue            0.2589684 9.994031e-01 1.000000e+00
## M3_brown           0.9595463 6.359708e-01 1.000000e+00
## M4_yellow          1.3943998 2.186229e-01 7.651803e-01
## M5_green           0.5604264 9.315386e-01 1.000000e+00
## M6_red            18.3563827 1.246918e-55 2.618528e-54
## M7_black           0.3145521 9.880536e-01 1.000000e+00
## M8_pink            2.0437365 2.899534e-02 1.522256e-01
## M9_magenta         4.1752756 1.103923e-06 7.727462e-06
## M10_purple         0.7885069 7.575422e-01 1.000000e+00
## M11_greenyellow    0.2070003 9.922681e-01 1.000000e+00
## M12_tan            1.0815100 5.104906e-01 1.000000e+00
## M13_salmon         0.0000000 1.000000e+00 1.000000e+00
## M14_cyan           1.3124825 3.778501e-01 1.000000e+00
## M15_midnightblue   1.0556558 5.514536e-01 1.000000e+00
## M16_lightcyan      0.7316755 7.628255e-01 1.000000e+00
```

```
## M17_grey60        6.8665689 1.456634e-08 1.529466e-07
## M18_lightgreen    2.5198636 3.990386e-02 1.675962e-01
## M19_lightyellow   0.8142841 7.097983e-01 1.000000e+00
## M20_royalblue     1.2667870 4.333959e-01 1.000000e+00
## M21_darkred       0.9096507 6.520517e-01 1.000000e+00
```

At the level of modules, test non-zero and zero modules for enrichment in broadly expressed, blood, brain, or lymphocyte modules

```r
fname = "Subgrp_STRUCTresultMEfMRIcorr_bootlim_data4plotting_LV1_ci95.csv"
fname = here("PLSresults",fname)
plsbootdata = read.csv(fname)


var2use = "nonzero"


td_tmp = subset(plsbootdata, plsbootdata$Grp=="TD")
rownames(td_tmp) = 1:nmods
poor_tmp = subset(plsbootdata, plsbootdata$Grp=="Poor")
rownames(poor_tmp) = 1:nmods
good_tmp = subset(plsbootdata, plsbootdata$Grp=="Good")
rownames(good_tmp) = 1:nmods


td_mods = as.numeric(rownames(td_tmp)[td_tmp[,var2use]==1])
asd_poor_mods = as.numeric(rownames(poor_tmp)[poor_tmp[,var2use]==1])
asd_good_mods = as.numeric(rownames(good_tmp)[good_tmp[,var2use]==1])
if (identical(td_mods,numeric(0))){
  td_mods = NA
} else if (identical(asd_poor_mods,numeric(0))){
  asd_poor_mods = NA
} else if (identical(asd_good_mods,numeric(0))){
  asd_good_mods = NA
}


mask = logical(length = nmods)
nonzero_mods = sort(unique(c(td_mods, asd_poor_mods, asd_good_mods)))
mask[nonzero_mods] = TRUE
zero_mods = 1:nrow(td_tmp)
zero_mods = zero_mods[!mask]


nz_mods = mod_names[nonzero_mods]
z_mods = mod_names[zero_mods]


# broadly expressed modules
broadmods = mod_names[out_mats$BroadGenes$fdr<=fdr_thresh]; broadmods
```

```
## [1] "M1_turquoise"     "M2_blue"          "M8_pink"
## [4] "M10_purple"       "M11_greenyellow"  "M13_salmon"
## [7] "M15_midnightblue" "M18_lightgreen"   "M21_darkred"
```

```r
# test enrichment between non-zero modules and broadly expressed modules
overlap_res = genelistOverlap(nz_mods,
                              broadmods,
```

```
                                     length(mod_names),
                                     print_result = TRUE)
```

[1] "OR = 184.500000, p = 0.000187"

```
# test enrichment between zero modules and broadly expressed modules
overlap_res = genelistOverlap(z_mods,
                              broadmods,
                              length(mod_names),
                              print_result = TRUE)
```

[1] "OR = 0.000000, p = 1.000000"

```
# blood modules
bloodmods = mod_names[out_mats$BloodGenes$fdr<=fdr_thresh]

# test enrichment between non-zero modules and blood modules
overlap_res = genelistOverlap(nz_mods,
                              bloodmods,
                              length(mod_names),
                              print_result = TRUE)
```

[1] "OR = 0.600000, p = 0.964912"

```
# test enrichment between zero modules and blood modules
overlap_res = genelistOverlap(z_mods,
                              bloodmods,
                              length(mod_names),
                              print_result = TRUE)
```

[1] "OR = 8.571429, p = 0.255639"

```
# brain expressed modules
brainmods = mod_names[out_mats$BrainGenes$fdr<=fdr_thresh]

# test enrichment between non-zero modules and brain modules
overlap_res = genelistOverlap(nz_mods,
                              brainmods,
                              length(mod_names),
                              print_result = TRUE)
```

[1] "OR = 0.000000, p = 1.000000"

```
# test enrichment between zero modules and brain modules
overlap_res = genelistOverlap(z_mods,
                              brainmods,
                              length(mod_names),
                              print_result = TRUE)
```

[1] "OR = 4.555556, p = 0.476190"

```
# lymphocyte modules
lymphocytemods = mod_names[out_mats$LymphocyteGenes$fdr<=fdr_thresh]

# test enrichment between non-zero modules and lymphocyte modules
overlap_res = genelistOverlap(nz_mods,
                              lymphocytemods,
                              length(mod_names),
```

```
                                  print_result = TRUE)
```

```
## [1] "OR = 4.444444, p = 0.537594"
```

```
# test enrichment between zero modules and lymphocyte modules
overlap_res = genelistOverlap(z_mods,
                              lymphocytemods,
                              length(mod_names),
                              print_result = TRUE)
```

```
## [1] "OR = 1.055556, p = 0.875940"
```

At the level of modules, test for overlap between non-zero modules across groups

```
# show the ASD Poor modules
asd_poor_mods = mod_names[asd_poor_mods]

# show the ASD Good modules
asd_good_mods = mod_names[asd_good_mods]

# show the TD modules
td_mods = mod_names[td_mods]

# test overlap between ASD Poor and ASD Good
overlap_res = genelistOverlap(asd_poor_mods,
                              asd_good_mods,
                              length(mod_names),
                              print_result = TRUE)
```

```
## [1] "OR = 0.000000, p = 1.000000"
```

```
# test overlap between TD and ASD Good
overlap_res = genelistOverlap(td_mods,
                              asd_good_mods,
                              length(mod_names),
                              print_result = TRUE)
```

```
## [1] "OR = 0.000000, p = 1.000000"
```

```
# test overlap between TD and ASD Poor
overlap_res = genelistOverlap(td_mods,
                              asd_poor_mods,
                              length(mod_names),
                              print_result = TRUE)
```

```
## [1] "OR = 1.666667, p = 0.655659"
```

Examine enrichment between gene classes and non-zero or zero modules

```r
geneclasses = c("BroadGenes","BloodGenes","BrainGenes","LymphocyteGenes")
res_colnames = c("Non-Zero Modules","Zero Modules")

ORmat = data.frame(matrix(nrow = length(geneclasses),
                          ncol = length(res_colnames)))
logPmat = data.frame(matrix(nrow = length(geneclasses),
                            ncol = length(res_colnames)))
Pmat = data.frame(matrix(nrow = length(geneclasses),
                         ncol = length(res_colnames)))
FDRmat = data.frame(matrix(nrow = length(geneclasses),
                           ncol = length(res_colnames)))

colnames(ORmat) = res_colnames
colnames(logPmat) = res_colnames
colnames(Pmat) = res_colnames
colnames(FDRmat) = res_colnames
rownames(ORmat) = geneclasses
rownames(logPmat) = geneclasses
rownames(Pmat) = geneclasses
rownames(FDRmat) = geneclasses

for (i in 1:length(geneclasses)){
  # intersect genes2 with background list
  genes2 = eval(as.name(geneclasses[i]))
  mask = is.element(genes2,bglist)
  genes2 = data.frame(genes2[mask])

  overlap_res = genelistOverlap(nz_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,1] = overlap_res[[1]]$OR
  logPmat[i,1] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,1] = overlap_res[[1]]$hypergeo_p

  overlap_res = genelistOverlap(z_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,2] = overlap_res[[1]]$OR
  logPmat[i,2] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,2] = overlap_res[[1]]$hypergeo_p
}
for (i in 1:dim(Pmat)[2]){
  FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
}
```

```
zLIM = c(0,30)
par(mar = c(6, 8.5, 3, 3))
WGCNA::labeledHeatmap(Matrix = logPmat,
                      xLabels = colnames(ORmat),
                      yLabels = rownames(ORmat),
                      ySymbols = NULL,
                      colorLabels = FALSE,
                      colors = WGCNA::blueWhiteRed(100),
                      textMatrix = round(ORmat, digits = 2),
                      setStdMargins = FALSE,
                      cex.text = 3,
                      zlim = zLIM)
```



```
# Enrichment Odds Ratios
ORmat
```
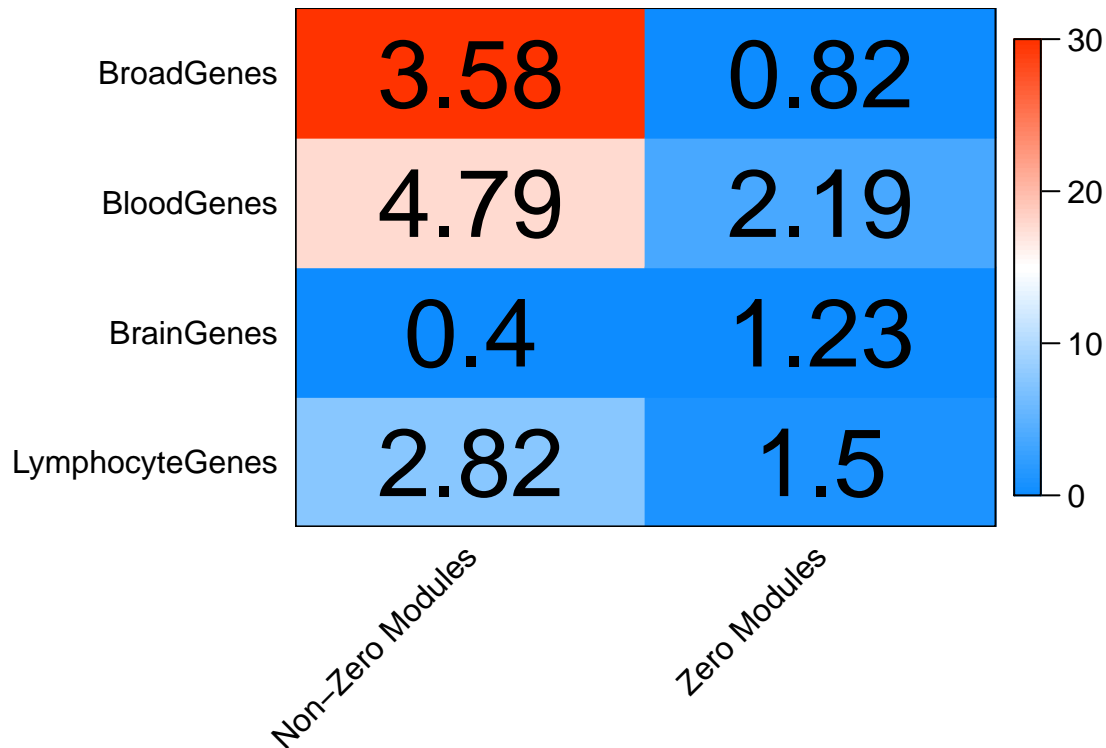
```
##               Non-Zero Modules Zero Modules
## BroadGenes          3.5847421    0.8168439
## BloodGenes          4.7909589    2.1907949
## BrainGenes          0.3984724    1.2301995
## LymphocyteGenes     2.8233783    1.5007987
```

```
# P-values
Pmat
```

```
##               Non-Zero Modules Zero Modules
## BroadGenes          1.480874e-93 1.0000000000
## BloodGenes          1.573773e-18 0.0001826812
## BrainGenes          1.000000e+00 0.5228156458
## LymphocyteGenes     1.944252e-08 0.1012197835
```

```
# FDR
FDRmat
```

```
##                  Non-Zero Modules Zero Modules
## BroadGenes         5.923497e-93 1.0000000000
## BloodGenes         3.147546e-18 0.0007307249
## BrainGenes         1.000000e+00 0.6970875277
## LymphocyteGenes    2.592336e-08 0.2024395670
```

Examine enrichment between DE song bird, ASD HC, ASD SFARI, Parikshak ASD DE modules, and human accelerated genes and non-zero or zero modules

```r
geneclasses = list(SongBirdDE,
                   HumanSpecific1,
                   HumanSpecific2,
                   ASDPrenatal1,
                   ASDPrenatal2,
                   ASDCTXDownreg,
                   ASDCTXUpreg,
                   ASDPTVs,
                   ASDPTVs_pLI,
                   SFARIASD,
                   FMRP1,
                   FMRP2,
                   CHD81,
                   CHD82)

geneclassnames = c("Song Bird DE",
                   "Human-Specific1",
                   "Human-Specific2",
                   "ASD Prenatal1",
                   "ASD Prenatal2",
                   "ASD CTX Downreg",
                   "ASD CTX Upreg",
                   "ASD dnPTVs",
                   "ASD dnPTVs + pLI >= 0.9",
                   "SFARI ASD",
                   "FMRP Targets1",
                   "FMRP Targets2",
                   "CHD8 Targets1",
                   "CHD8 Targets2")

res_colnames =  c("Broadly Expressed","Non-Zero Modules","Zero Modules")
ORmat = data.frame(matrix(nrow = length(geneclasses),
                          ncol = length(res_colnames)))
logPmat = data.frame(matrix(nrow = length(geneclasses),
                            ncol = length(res_colnames)))
Pmat = data.frame(matrix(nrow = length(geneclasses),
                         ncol = length(res_colnames)))
FDRmat = data.frame(matrix(nrow = length(geneclasses),
```

```r
                                ncol = length(res_colnames)))
colnames(ORmat) = res_colnames
colnames(logPmat) = res_colnames
colnames(Pmat) = res_colnames
colnames(FDRmat) = res_colnames
rownames(ORmat) = geneclassnames
rownames(logPmat) = geneclassnames
rownames(Pmat) = geneclassnames
rownames(FDRmat) = geneclassnames

for (i in 1:length(geneclasses)){
  # intersect with background list
  genes2 = geneclasses[[i]]
  mask = is.element(genes2,bglist)
  genes2 = data.frame(genes2[mask])

  overlap_res = genelistOverlap(BroadGenes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,1] = overlap_res[[1]]$OR
  logPmat[i,1] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,1] = overlap_res[[1]]$hypergeo_p

  overlap_res = genelistOverlap(nz_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,2] = overlap_res[[1]]$OR
  logPmat[i,2] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,2] = overlap_res[[1]]$hypergeo_p

  overlap_res = genelistOverlap(z_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,3] = overlap_res[[1]]$OR
  logPmat[i,3] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,3] = overlap_res[[1]]$hypergeo_p
}
for (i in 1:dim(Pmat)[2]){
  FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
}


zLIM = c(0,-log10(0.005))
par(mar = c(6, 8.5, 3, 3))
WGCNA::labeledHeatmap(Matrix = logPmat,
                      xLabels = colnames(ORmat),
                      yLabels = rownames(ORmat),
```
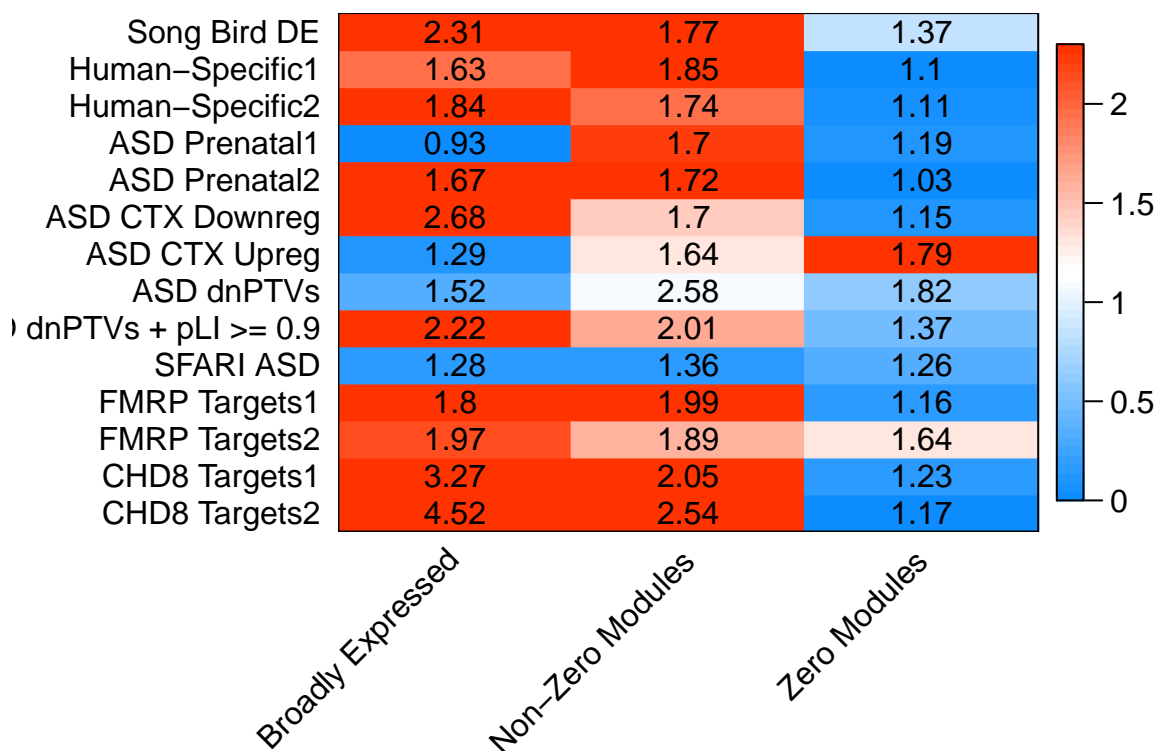
```
                    ySymbols = NULL,
                    colorLabels = FALSE,
                    colors = WGCNA::blueWhiteRed(50),
                    textMatrix = round(ORmat, digits = 2),
                    setStdMargins = FALSE,
                    cex.text = 1,
                    zlim = zLIM)
```

	Broadly Expressed	Non–Zero Modules	Zero Modules
Song Bird DE	2.31	1.77	1.37
Human–Specific1	1.63	1.85	1.1
Human–Specific2	1.84	1.74	1.11
ASD Prenatal1	0.93	1.7	1.19
ASD Prenatal2	1.67	1.72	1.03
ASD CTX Downreg	2.68	1.7	1.15
ASD CTX Upreg	1.29	1.64	1.79
ASD dnPTVs	1.52	2.58	1.82
dnPTVs + pLI >= 0.9	2.22	2.01	1.37
SFARI ASD	1.28	1.36	1.26
FMRP Targets1	1.8	1.99	1.16
FMRP Targets2	1.97	1.89	1.64
CHD8 Targets1	3.27	2.05	1.23
CHD8 Targets2	4.52	2.54	1.17

```
# Enrichment Odds Ratios
ORmat
```

```
##                         Broadly Expressed Non-Zero Modules Zero Modules
## Song Bird DE                     2.313688         1.766018     1.367557
## Human-Specific1                  1.631961         1.849270     1.098895
## Human-Specific2                  1.838675         1.737814     1.110486
## ASD Prenatal1                    0.926925         1.703069     1.188698
## ASD Prenatal2                    1.670964         1.723063     1.026814
## ASD CTX Downreg                  2.680746         1.698674     1.146462
## ASD CTX Upreg                    1.285018         1.643444     1.792725
## ASD dnPTVs                       1.518109         2.579444     1.822494
## ASD dnPTVs + pLI >= 0.9          2.224350         2.010678     1.369595
## SFARI ASD                        1.280636         1.357698     1.263160
## FMRP Targets1                    1.797595         1.988684     1.164068
## FMRP Targets2                    1.967917         1.891329     1.637426
## CHD8 Targets1                    3.270380         2.052746     1.233921
## CHD8 Targets2                    4.519513         2.543460     1.167394
```

```
# P-values
Pmat
```

```
##                 Broadly Expressed Non-Zero Modules Zero Modules
```

```
## Song Bird DE                 1.207256e-12      2.931725e-03 0.1368211698
## Human-Specific1              1.121700e-02      1.454892e-04 0.9326513736
## Human-Specific2              3.930965e-04      1.157684e-02 0.8584468499
## ASD Prenatal1                1.000000e+00      5.633423e-03 0.7471413303
## ASD Prenatal2                3.797020e-03      4.664096e-03 0.9902083264
## ASD CTX Downreg              2.357339e-13      3.556493e-02 0.7510873768
## ASD CTX Upreg                8.001010e-01      5.025116e-02 0.0000280431
## ASD dnPTVs                   4.664012e-01      8.499079e-02 0.2420677095
## ASD dnPTVs + pLI >= 0.9      2.704798e-03      2.351178e-02 0.3230860055
## SFARI ASD                    7.123606e-01      6.624826e-01 0.4480139650
## FMRP Targets1                3.146039e-03      2.511948e-04 0.7045078476
## FMRP Targets2                7.574835e-03      2.692390e-02 0.0483558183
## CHD8 Targets1                2.526525e-66      1.922342e-11 0.6731317925
## CHD8 Targets2                3.046940e-176     5.203285e-35 0.9979914178
```

```
FDRmat
```

```
##                        Broadly Expressed Non-Zero Modules Zero Modules
## Song Bird DE                4.225398e-12      8.208830e-03 0.6384987923
## Human-Specific1             1.570380e-02      6.789495e-04 0.9979914178
## Human-Specific2             1.100670e-03      2.025946e-02 0.9979914178
## ASD Prenatal1               1.000000e+00      1.126685e-02 0.9979914178
## ASD Prenatal2               6.644784e-03      1.088289e-02 0.9979914178
## ASD CTX Downreg             1.100092e-12      4.526446e-02 0.9979914178
## ASD CTX Upreg               8.616473e-01      5.862636e-02 0.0003926034
## ASD dnPTVs                  5.936015e-01      9.152854e-02 0.8472369833
## ASD dnPTVs + pLI >= 0.9     6.292077e-03      3.657388e-02 0.9046408153
## SFARI ASD                   8.310873e-01      6.624826e-01 0.9979914178
## FMRP Targets1               6.292077e-03      8.791818e-04 0.9979914178
## FMRP Targets2               1.178308e-02      3.769346e-02 0.3384907284
## CHD8 Targets1               1.768568e-65      1.345639e-10 0.9979914178
## CHD8 Targets2               4.265716e-175     7.284599e-34 0.9979914178
```

Assess enrichments by specific modules

```r
geneclasses = list(SongBirdDE,
                   HumanSpecific1,
                   HumanSpecific2,
                   ASDPrenatal1,
                   ASDPrenatal2,
                   ASDCTXDownreg,
                   ASDCTXUpreg,
                   ASDPTVs,
                   ASDPTVs_pLI,
                   SFARIASD,
                   FMRP1,
                   FMRP2,
                   CHD81,
                   CHD82)

geneclassnames = c("Song Bird DE",
                   "Human-Specific1",
```

```r
                  "Human-Specific2",
                  "ASD Prenatal1",
                  "ASD Prenatal2",
                  "ASD CTX Downreg",
                  "ASD CTX Upreg",
                  "ASD dnPTVs",
                  "ASD dnPTVs + pLI >= 0.9",
                  "SFARI ASD",
                  "FMRP Targets1",
                  "FMRP Targets2",
                  "CHD8 Targets1",
                  "CHD8 Targets2")

ORmat = data.frame(matrix(nrow = length(mod_names),
                          ncol = length(geneclasses)))
colnames(ORmat) = geneclassnames
rownames(ORmat) = mod_names

Pmat = data.frame(matrix(nrow = length(mod_names),
                         ncol = length(geneclasses)))
colnames(Pmat) = geneclassnames
rownames(Pmat) = mod_names

FDRmat = data.frame(matrix(nrow = length(mod_names),
                           ncol = length(geneclasses)))
colnames(FDRmat) = geneclassnames
rownames(FDRmat) = mod_names

for (imod in 1:length(mod_names)){
  for (igc in 1:length(geneclasses)){
    # intersect geneclass list with background
    genes2 = geneclasses[[igc]]
    mask = is.element(genes2,bglist)
    genes2 = data.frame(genes2[mask])

    modulegenes = wgcna_res$geneSymbol[wgcna_res$moduleLabels==imod]

    overlap_res = genelistOverlap(modulegenes,
                                  genes2,
                                  backgroundTotal,
                                  print_result = FALSE,
                                  header = FALSE)
    ORmat[imod,igc] = overlap_res[[1]]$OR
    Pmat[imod,igc] = overlap_res[[1]]$hypergeo_p
  }
}
for (i in 1:dim(Pmat)[2]){
  FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
}

# Enrichment Odds Ratios
ORmat

##                 Song Bird DE Human-Specific1 Human-Specific2
```

```
## M1_turquoise        1.4445211       1.3602330       1.3827322
## M2_blue             0.7958297       1.4650369       1.2453501
## M3_brown            0.8860220       0.6767508       0.5936064
## M4_yellow           1.5090185       1.2511181       0.8326079
## M5_green            0.9253541       0.6903564       0.1652351
## M6_red              0.6901101       0.6560055       0.4810582
## M7_black            1.1156977       1.0673586       1.2112116
## M8_pink             1.6308335       1.2989832       0.6435447
## M9_magenta          0.5923608       1.1530506       1.5941173
## M10_purple          2.4734411       0.7101442       1.0631122
## M11_greenyellow     0.8497899       1.0677513       0.5077765
## M12_tan             0.7903243       1.4725596       1.9683535
## M13_salmon          1.0511399       2.2164479       2.1740584
## M14_cyan            1.5767099       0.9321128       0.9290233
## M15_midnightblue    1.3406242       1.6501061       1.8071866
## M16_lightcyan       0.9097010       0.9637196       1.3902530
## M17_grey60          0.6704924       0.3662373       1.0617409
## M18_lightgreen      1.4162710       1.6715831       1.3469630
## M19_lightyellow     1.5875813       0.6238701       0.6583452
## M20_royalblue       2.4333866       0.1017561       0.8521449
## M21_darkred         0.9900495       1.7789470       2.8840875
##                  ASD Prenatal1 ASD Prenatal2 ASD CTX Downreg ASD CTX Upreg
## M1_turquoise        1.3381209    1.21649298       1.1577181     2.6647637
## M2_blue             0.1370147    0.67341820       1.4019170     0.3555503
## M3_brown            1.2149589    1.01679360       0.5383083     0.4253381
## M4_yellow           0.6147053    1.18654720       0.9227490     1.1016428
## M5_green            0.7392235    0.69232381       0.8860065     0.3617998
## M6_red              0.3301020    0.62262775       0.5391205     0.6774242
## M7_black            0.2859428    0.45985351       0.9222863     1.9704467
## M8_pink             0.1732171    0.46607986       1.0240332     0.1920415
## M9_magenta          0.3930965    0.56751762       0.7069401     4.3941300
## M10_purple          8.2872987    3.79826082       1.7183441     1.2261200
## M11_greenyellow     0.3378921    1.07248377       0.7665975     0.3881439
## M12_tan             0.5707456    0.35478149       0.6613822     2.4172766
## M13_salmon          0.7978864    1.33216464       1.4362206     0.4104708
## M14_cyan            2.6667225    2.36212561       2.5407476     0.9872183
## M15_midnightblue    3.8293530    3.80990783       2.1158332     0.6532845
## M16_lightcyan       0.5241799    0.25869606       0.9575429     2.4324639
## M17_grey60          1.1131640    1.01525923       0.9575429     0.9793079
## M18_lightgreen      2.3316823    1.34855662       1.7337107     0.1452521
## M19_lightyellow     0.4108537    0.09432708       1.2952068     0.9290014
## M20_royalblue       8.6813664    2.92346826       2.0571087     0.6227430
## M21_darkred         0.8633273    0.54799867       1.4525683     0.5045455
##                  ASD dnPTVs ASD dnPTVs + pLI >= 0.9 SFARI ASD
## M1_turquoise       2.331068               1.8123249 1.0941257
## M2_blue            0.000000               0.0000000 0.5267210
## M3_brown           1.071075               0.9634694 1.2063686
## M4_yellow          1.385108               1.5128977 1.0624673
## M5_green           0.000000               0.5071179 0.6020550
## M6_red             0.000000               0.0000000 0.7762389
## M7_black           1.643202               0.8734169 0.8276617
## M8_pink            1.818251               0.6382691 0.4496127
## M9_magenta         0.000000               1.0708560 0.4978471
## M10_purple        12.087633               9.2202576 4.0020135
```

```
## M11_greenyellow    0.000000              0.0000000 0.3568258
## M12_tan            4.598326              1.1743421 0.7333386
## M13_salmon          0.000000              1.2258483 0.1871304
## M14_cyan            3.348805              2.4203375 2.6490852
## M15_midnightblue    0.000000              0.6297367 2.5329171
## M16_lightcyan       0.000000              0.0000000 1.2779503
## M17_grey60          0.000000              0.6614501 1.6143994
## M18_lightgreen      0.000000              1.4690321 0.6853322
## M19_lightyellow     0.000000              0.0000000 1.0564072
## M20_royalblue       4.336976              4.0008475 1.8469824
## M21_darkred         0.000000              0.0000000 0.0000000
##                   FMRP Targets1 FMRP Targets2 CHD8 Targets1 CHD8 Targets2
## M1_turquoise        1.77837177      1.4218235     1.4026976     1.0273298
## M2_blue             0.09058257      0.4497145     0.9584927     2.2386635
## M3_brown            0.97644260      1.5487484     0.7002422     0.6495313
## M4_yellow           0.28219918      0.5176744     1.9441924     2.3620897
## M5_green            0.60067026      1.2995524     1.1431016     1.5181749
## M6_red              0.07748698      1.3882459     0.6686003     1.4838831
## M7_black            1.04856065      2.1665335     0.6734572     0.4274248
## M8_pink             0.18366396      0.2232252     1.3907819     4.0816199
## M9_magenta          0.10105717      1.2779379     0.6816482     0.5346531
## M10_purple          6.57738001      5.2056148     3.2020846     2.5922017
## M11_greenyellow     0.10937463      0.0000000     0.9915956     2.0356069
## M12_tan             1.29703596      1.4024827     0.5250000     0.4607735
## M13_salmon          1.89878988      0.5699903     1.7081370     1.5627897
## M14_cyan            1.23884272      1.7002110     2.2693241     2.4702393
## M15_midnightblue    4.61389446      3.8651593     2.3011600     2.0559087
## M16_lightcyan       0.78642271      0.9458535     0.3754422     0.2151048
## M17_grey60          0.78642271      0.0000000     0.8627102     0.2908104
## M18_lightgreen      0.86252813      1.5737302     1.5458041     2.0696739
## M19_lightyellow     0.65084682      1.0526434     0.4203669     0.3281622
## M20_royalblue       6.75317693      0.5324469     2.3867476     2.0317321
## M21_darkred         0.47984278      1.7883298     1.5658605     1.2546882
```

P-values
Pmat

```
##                   Song Bird DE Human-Specific1 Human-Specific2
## M1_turquoise      1.135926e-02    0.0370449781    0.0531442710
## M2_blue           9.377147e-01    0.0126259601    0.1935379709
## M3_brown          8.102005e-01    0.9883005346    0.9896875497
## M4_yellow         2.728203e-02    0.1653906610    0.8194122762
## M5_green          7.092930e-01    0.9685538226    0.9999974945
## M6_red            9.528888e-01    0.9769653059    0.9937242112
## M7_black          3.840173e-01    0.4545384863    0.2818489779
## M8_pink           1.758832e-02    0.1449957535    0.9421794458
## M9_magenta        9.733735e-01    0.3256260624    0.0490572469
## M10_purple        8.148640e-06    0.9302965559    0.4831616424
## M11_greenyellow   7.730565e-01    0.4579170004    0.9778899554
## M12_tan           8.381252e-01    0.0586074419    0.0057577949
## M13_salmon        4.907752e-01    0.0001038944    0.0016049040
## M14_cyan          7.659553e-02    0.6472804680    0.6400846002
## M15_midnightblue  2.164513e-01    0.0469912857    0.0487215926
## M16_lightcyan     6.632690e-01    0.6040681500    0.2254255378
## M17_grey60        8.823591e-01    0.9941921806    0.5047795745
```

```
## M18_lightgreen    1.834003e-01    0.0540509708    0.2672967510
## M19_lightyellow   9.966779e-02    0.9159692459    0.8575415339
## M20_royalblue     1.805791e-03    0.9999309678    0.7045897102
## M21_darkred       5.741872e-01    0.0415247676    0.0009591607
##                   ASD Prenatal1 ASD Prenatal2 ASD CTX Downreg ASD CTX Upreg
## M1_turquoise      4.066360e-02  2.722458e-01    0.470344698   5.389578e-18
## M2_blue           1.000000e+00  9.949803e-01    0.084889985   9.999913e-01
## M3_brown          1.667206e-01  5.748241e-01    0.990974520   9.997226e-01
## M4_yellow         9.951909e-01  2.436432e-01    0.686673625   4.150673e-01
## M5_green          9.581872e-01  9.704682e-01    0.730193394   9.996131e-01
## M6_red            9.999970e-01  9.872932e-01    0.976308498   9.445452e-01
## M7_black          9.999990e-01  9.992359e-01    0.674084136   1.306131e-03
## M8_pink           1.000000e+00  9.985516e-01    0.540636871   9.999752e-01
## M9_magenta        9.997949e-01  9.880782e-01    0.872129944   1.299903e-14
## M10_purple        4.015611e-49  4.904733e-15    0.039073174   2.761094e-01
## M11_greenyellow   9.999203e-01  4.481913e-01    0.815924947   9.958920e-01
## M12_tan           9.893399e-01  9.996371e-01    0.894379052   1.211472e-04
## M13_salmon        8.610099e-01  1.381745e-01    0.161605388   9.932632e-01
## M14_cyan          6.180530e-06  2.535122e-04    0.002704974   5.780211e-01
## M15_midnightblue  1.866337e-10  1.788732e-09    0.022910114   8.807543e-01
## M16_lightcyan     9.771761e-01  9.991133e-01    0.609303240   2.277237e-03
## M17_grey60        4.086077e-01  5.399646e-01    0.609303240   5.863878e-01
## M18_lightgreen    5.444295e-04  2.012199e-01    0.109400839   9.988837e-01
## M19_lightyellow   9.922097e-01  9.999668e-01    0.336696478   6.359043e-01
## M20_royalblue     2.902982e-26  2.469850e-05    0.042274031   8.837559e-01
## M21_darkred       7.197188e-01  9.471181e-01    0.251699190   9.351176e-01
##                   ASD dnPTVs ASD dnPTVs + pLI >= 0.9    SFARI ASD
## M1_turquoise      0.1017431544            2.250048e-02 6.101846e-01
## M2_blue           1.0000000000            1.000000e+00 9.827665e-01
## M3_brown          0.6270976927            6.254016e-01 3.392103e-01
## M4_yellow         0.5324191633            2.356721e-01 5.098157e-01
## M5_green          1.0000000000            9.105677e-01 9.241632e-01
## M6_red            1.0000000000            1.000000e+00 7.996989e-01
## M7_black          0.4725612191            6.834226e-01 7.487100e-01
## M8_pink           0.4388050788            8.283296e-01 9.643412e-01
## M9_magenta        1.0000000000            5.474334e-01 9.422390e-01
## M10_purple        0.0001377041            7.743579e-13 6.135478e-07
## M11_greenyellow   1.0000000000            1.000000e+00 9.766108e-01
## M12_tan           0.0801795280            4.861569e-01 8.027132e-01
## M13_salmon        1.0000000000            4.583188e-01 9.953270e-01
## M14_cyan          0.2688111675            9.433107e-02 1.067048e-02
## M15_midnightblue  1.0000000000            7.998837e-01 1.936296e-02
## M16_lightcyan     1.0000000000            1.000000e+00 3.956264e-01
## M17_grey60        1.0000000000            7.838677e-01 2.149659e-01
## M18_lightgreen    1.0000000000            4.046924e-01 7.926736e-01
## M19_lightyellow   1.0000000000            1.000000e+00 5.502525e-01
## M20_royalblue     0.2148570594            1.085325e-02 1.495658e-01
## M21_darkred       1.0000000000            1.000000e+00 1.000000e+00
##                   FMRP Targets1 FMRP Targets2 CHD8 Targets1 CHD8 Targets2
## M1_turquoise      2.226484e-04  1.474974e-01  2.984251e-03  9.969544e-01
## M2_blue           1.000000e+00  9.810569e-01  7.951487e-01  1.781877e-18
## M3_brown          6.298647e-01  1.357062e-01  9.983422e-01  9.999986e-01
## M4_yellow         9.996186e-01  9.341598e-01  3.453303e-07  3.641500e-15
## M5_green          9.593074e-01  3.267190e-01  2.527031e-01  3.054372e-04
```

```
## M6_red          9.999975e-01 2.712390e-01 9.960769e-01 8.703035e-04
## M7_black        5.102954e-01 2.641720e-02 9.943618e-01 1.000000e+00
## M8_pink         9.997783e-01 9.891998e-01 2.638276e-02 2.276259e-30
## M9_magenta      9.999479e-01 3.752907e-01 9.869745e-01 9.999973e-01
## M10_purple      7.335198e-21 1.061350e-07 2.968418e-16 1.466074e-13
## M11_greenyellow 9.998893e-01 1.000000e+00 5.910126e-01 1.147537e-07
## M12_tan         2.615079e-01 3.060536e-01 9.994199e-01 9.999999e-01
## M13_salmon      2.171335e-02 8.701578e-01 1.066555e-03 1.199621e-03
## M14_cyan        3.569345e-01 2.241826e-01 1.218388e-05 2.597814e-08
## M15_midnightblue 7.855050e-08 1.857350e-03 1.717384e-05 1.864293e-05
## M16_lightcyan   7.534806e-01 6.322221e-01 9.997070e-01 1.000000e+00
## M17_grey60      7.534806e-01 1.000000e+00 7.731854e-01 1.000000e+00
## M18_lightgreen  6.884989e-01 3.094799e-01 3.509229e-02 5.017636e-05
## M19_lightyellow 8.412809e-01 5.747735e-01 9.986039e-01 9.999997e-01
## M20_royalblue   1.216023e-11 8.498274e-01 3.321972e-05 1.035651e-04
## M21_darkred     9.204829e-01 2.474667e-01 3.948243e-02 1.581403e-01
```

```
# FDR
FDRmat
```

```
##                  Song Bird DE Human-Specific1 Human-Specific2
## M1_turquoise     0.0795148525  0.175822326     0.18600495
## M2_blue          0.9733735451  0.132572581     0.58061391
## M3_brown         0.9733735451  0.999930968     0.99999749
## M4_yellow        0.1145845372  0.385911542     0.99999749
## M5_green         0.9733735451  0.999930968     0.99999749
## M6_red           0.9733735451  0.999930968     0.99999749
## M7_black         0.8064362451  0.801354751     0.59188285
## M8_pink          0.0923387045  0.380613853     0.99999749
## M9_magenta       0.9733735451  0.683814731     0.18600495
## M10_purple       0.0001711214  0.999930968     0.88336426
## M11_greenyellow  0.9733735451  0.801354751     0.99999749
## M12_tan          0.9733735451  0.175822326     0.04030456
## M13_salmon       0.9369344138  0.002181782     0.01685149
## M14_cyan         0.2680843478  0.970920702     0.99999749
## M15_midnightblue 0.5050529741  0.175822326     0.18600495
## M16_lightcyan    0.9733735451  0.970920702     0.59174204
## M17_grey60       0.9733735451  0.999930968     0.88336426
## M18_lightgreen   0.4814257997  0.175822326     0.59188285
## M19_lightyellow  0.2990033553  0.999930968     0.99999749
## M20_royalblue    0.0189608037  0.999930968     0.99999749
## M21_darkred      0.9733735451  0.175822326     0.01685149
##                  ASD Prenatal1 ASD Prenatal2 ASD CTX Downreg ASD CTX Upreg
## M1_turquoise     1.423226e-01 7.146452e-01    0.95837883     1.131811e-16
## M2_blue          1.000000e+00 9.999668e-01    0.35653794     9.999913e-01
## M3_brown         5.001619e-01 9.999668e-01    0.99097452     9.999913e-01
## M4_yellow        1.000000e+00 7.146452e-01    0.95837883     9.999913e-01
## M5_green         1.000000e+00 9.999668e-01    0.95837883     9.999913e-01
## M6_red           1.000000e+00 9.999668e-01    0.99097452     9.999913e-01
## M7_black         1.000000e+00 9.999668e-01    0.95837883     6.857185e-03
## M8_pink          1.000000e+00 9.999668e-01    0.95837883     9.999913e-01
## M9_magenta       1.000000e+00 9.999668e-01    0.98852422     1.364898e-13
## M10_purple       8.432784e-48 1.029994e-13    0.22193867     9.663829e-01
## M11_greenyellow  1.000000e+00 9.999668e-01    0.98852422     9.999913e-01
## M12_tan          1.000000e+00 9.999668e-01    0.98852422     8.480307e-04
```

```
## M13_salmon          1.000000e+00  5.803327e-01        0.48481616  9.999913e-01
## M14_cyan            3.244778e-05  1.330939e-03        0.05680446  9.999913e-01
## M15_midnightblue    1.306436e-09  1.878168e-08        0.22193867  9.999913e-01
## M16_lightcyan       1.000000e+00  9.999668e-01        0.95837883  9.564394e-03
## M17_grey60          1.000000e+00  9.999668e-01        0.95837883  9.999913e-01
## M18_lightgreen      2.286604e-03  7.042696e-01        0.38290294  9.999913e-01
## M19_lightyellow     1.000000e+00  9.999668e-01        0.78562512  9.999913e-01
## M20_royalblue       3.048131e-25  1.728895e-04        0.22193867  9.999913e-01
## M21_darkred         1.000000e+00  9.999668e-01        0.66071037  9.999913e-01
##                   ASD dnPTVs ASD dnPTVs + pLI >= 0.9   SFARI ASD
## M1_turquoise      0.712202081             1.575033e-01 1.0000000000
## M2_blue           1.000000000             1.000000e+00 1.0000000000
## M3_brown          1.000000000             1.000000e+00 1.0000000000
## M4_yellow         1.000000000             9.898230e-01 1.0000000000
## M5_green          1.000000000             1.000000e+00 1.0000000000
## M6_red            1.000000000             1.000000e+00 1.0000000000
## M7_black          1.000000000             1.000000e+00 1.0000000000
## M8_pink           1.000000000             1.000000e+00 1.0000000000
## M9_magenta        1.000000000             1.000000e+00 1.0000000000
## M10_purple        0.002891785             1.626152e-11 0.0000128845
## M11_greenyellow   1.000000000             1.000000e+00 1.0000000000
## M12_tan           0.712202081             1.000000e+00 1.0000000000
## M13_salmon        1.000000000             1.000000e+00 1.0000000000
## M14_cyan          1.000000000             4.952381e-01 0.1120399904
## M15_midnightblue  1.000000000             1.000000e+00 0.1355407283
## M16_lightcyan     1.000000000             1.000000e+00 1.0000000000
## M17_grey60        1.000000000             1.000000e+00 0.9028567788
## M18_lightgreen    1.000000000             1.000000e+00 1.0000000000
## M19_lightyellow   1.000000000             1.000000e+00 1.0000000000
## M20_royalblue     1.000000000             1.139592e-01 0.7852201971
## M21_darkred       1.000000000             1.000000e+00 1.0000000000
##                   FMRP Targets1 FMRP Targets2 CHD8 Targets1 CHD8 Targets2
## M1_turquoise       1.168904e-03  6.194891e-01  8.952754e-03  1.000000e+00
## M2_blue            1.000000e+00  1.000000e+00  9.997070e-01  1.870970e-17
## M3_brown           1.000000e+00  6.194891e-01  9.997070e-01  1.000000e+00
## M4_yellow          1.000000e+00  1.000000e+00  3.625968e-06  2.549050e-14
## M5_green           1.000000e+00  6.237362e-01  4.824332e-01  6.414182e-04
## M6_red             1.000000e+00  6.237362e-01  9.997070e-01  1.661489e-03
## M7_black           1.000000e+00  1.849204e-01  9.997070e-01  1.000000e+00
## M8_pink            1.000000e+00  1.000000e+00  6.925475e-02  4.780143e-29
## M9_magenta         1.000000e+00  6.567587e-01  9.997070e-01  1.000000e+00
## M10_purple         1.540392e-19  2.228834e-06  6.233677e-15  7.696889e-13
## M11_greenyellow    1.000000e+00  1.000000e+00  9.997070e-01  4.016379e-07
## M12_tan            9.152778e-01  6.237362e-01  9.997070e-01  1.000000e+00
## M13_salmon         9.119606e-02  1.000000e+00  3.732942e-03  2.099336e-03
## M14_cyan           1.000000e+00  6.237362e-01  8.528716e-05  1.091082e-07
## M15_midnightblue   5.498535e-07  1.950218e-02  9.016265e-05  5.592878e-05
## M16_lightcyan      1.000000e+00  9.483331e-01  9.997070e-01  1.000000e+00
## M17_grey60         1.000000e+00  1.000000e+00  9.997070e-01  1.000000e+00
## M18_lightgreen     1.000000e+00  6.237362e-01  8.188200e-02  1.317129e-04
## M19_lightyellow    1.000000e+00  9.284803e-01  9.997070e-01  1.000000e+00
## M20_royalblue      1.276825e-10  1.000000e+00  1.395228e-04  2.416519e-04
## M21_darkred        1.000000e+00  6.237362e-01  8.291310e-02  2.554575e-01
```

Examine enrichment between DE song bird, ASD HC, ASD SFARI, Parikshak ASD DE modules, and human accelerated genes and non-zero or zero modules

```r
geneclasses = list(SongBirdDE_notBE,
                   HumanSpecific1_notBE,
                   HumanSpecific2_notBE,
                   ASDPrenatal1_notBE,
                   ASDPrenatal2_notBE,
                   ASDCTXDownreg_notBE,
                   ASDCTXUpreg_notBE,
                   ASDPTVs_pLI_notBE,
                   SFARIASD_notBE,
                   FMRP1_notBE,
                   FMRP2_notBE,
                   CHD81_notBE,
                   CHD82_notBE)

geneclassnames = c("Song Bird DE",
                   "Human-Specific1",
                   "Human-Specific2",
                   "ASD Prenatal1",
                   "ASD Prenatal2",
                   "ASD CTX Downreg",
                   "ASD CTX Upreg",
                   "ASD dnPTVs + pLI >= 0.9",
                   "SFARI ASD",
                   "FMRP Targets1",
                   "FMRP Targets2",
                   "CHD8 Targets1",
                   "CHD8 Targets2")

res_colnames = c("Non-Zero Modules","Zero Modules")
ORmat = data.frame(matrix(nrow = length(geneclasses),
                          ncol = length(res_colnames)))
logPmat = data.frame(matrix(nrow = length(geneclasses),
                            ncol = length(res_colnames)))
Pmat = data.frame(matrix(nrow = length(geneclasses),
                         ncol = length(res_colnames)))
FDRmat = data.frame(matrix(nrow = length(geneclasses),
                           ncol = length(res_colnames)))
colnames(ORmat) = res_colnames
colnames(logPmat) = res_colnames
colnames(Pmat) = res_colnames
colnames(FDRmat) = res_colnames
rownames(ORmat) = geneclassnames
rownames(logPmat) = geneclassnames
rownames(Pmat) = geneclassnames
rownames(FDRmat) = geneclassnames

for (i in 1:length(geneclasses)){
  # intersect with background list
```

```r
    genes2 = geneclasses[[i]]
    mask = is.element(genes2,bglist)
    genes2 = data.frame(genes2[mask])

    overlap_res = genelistOverlap(nz_genes,
                                  genes2,
                                  backgroundTotal,
                                  print_result = FALSE,
                                  header = FALSE)
    ORmat[i,1] = overlap_res[[1]]$OR
    logPmat[i,1] = -log10(overlap_res[[1]]$hypergeo_p)
    Pmat[i,1] = overlap_res[[1]]$hypergeo_p

    overlap_res = genelistOverlap(z_genes,
                                  genes2,
                                  backgroundTotal,
                                  print_result = FALSE,
                                  header = FALSE)
    ORmat[i,2] = overlap_res[[1]]$OR
    logPmat[i,2] = -log10(overlap_res[[1]]$hypergeo_p)
    Pmat[i,2] = overlap_res[[1]]$hypergeo_p
}
for (i in 1:dim(Pmat)[2]){
  FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
}

zLIM = c(0,-log10(0.005))
par(mar = c(6, 8.5, 3, 3))
WGCNA::labeledHeatmap(Matrix = logPmat,
                      xLabels = colnames(ORmat),
                      yLabels = rownames(ORmat),
                      ySymbols = NULL,
                      colorLabels = FALSE,
                      colors = WGCNA::blueWhiteRed(50),
                      textMatrix = round(ORmat, digits = 2),
                      setStdMargins = FALSE,
                      cex.text = 1,
                      zlim = zLIM)
```
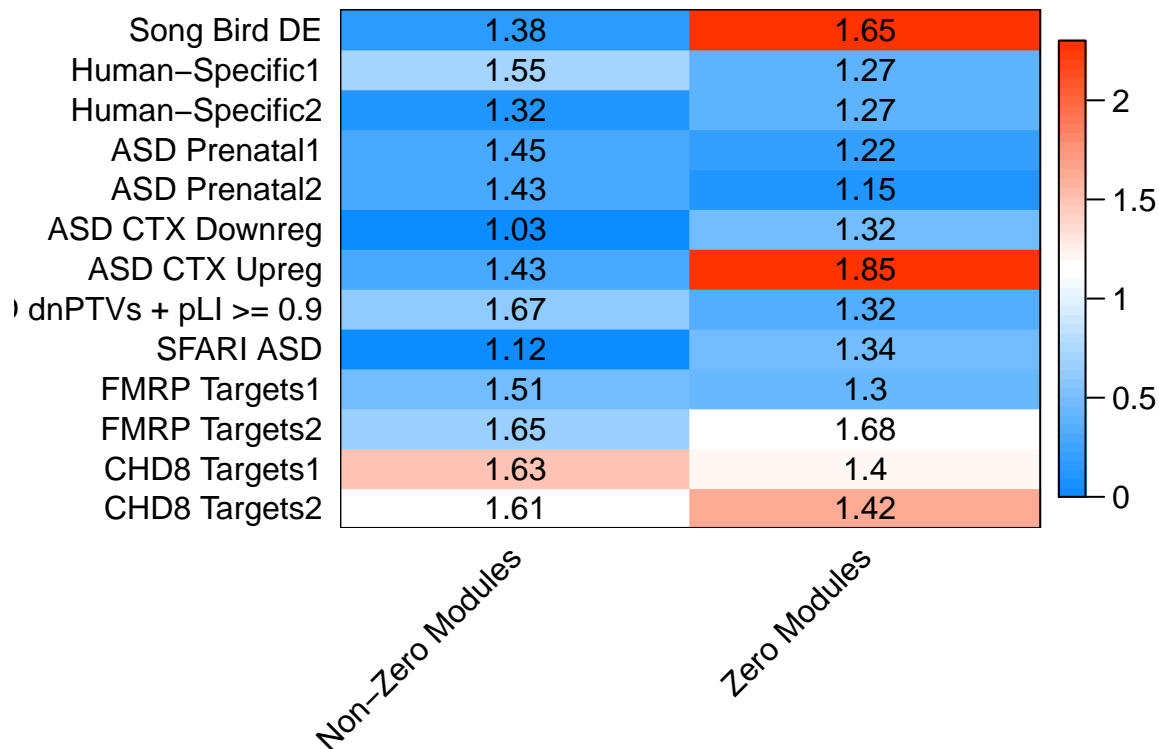
```
# Enrichment Odds Ratios
ORmat
```

```
##                       Non-Zero Modules Zero Modules
## Song Bird DE                  1.379753     1.651039
## Human-Specific1              1.546674     1.270655
## Human-Specific2              1.317637     1.269140
## ASD Prenatal1                1.450761     1.216592
## ASD Prenatal2                1.432734     1.148539
## ASD CTX Downreg              1.033342     1.319874
## ASD CTX Upreg                1.430286     1.847027
## ASD dnPTVs + pLI >= 0.9      1.669721     1.315668
## SFARI ASD                    1.121266     1.343655
## FMRP Targets1                1.514483     1.301697
## FMRP Targets2                1.653905     1.681547
## CHD8 Targets1                1.631681     1.402352
## CHD8 Targets2                1.614453     1.423758
```

```
# P-values
Pmat
```

```
##                       Non-Zero Modules Zero Modules
## Song Bird DE               0.65830774 2.955475e-03
## Human-Specific1            0.18486378 4.038351e-01
## Human-Specific2            0.78588124 4.213025e-01
## ASD Prenatal1              0.48435786 6.115897e-01
## ASD Prenatal2              0.52157849 7.921408e-01
## ASD CTX Downreg            0.99378945 3.313699e-01
## ASD CTX Upreg              0.50833829 6.246612e-05
## ASD dnPTVs + pLI >= 0.9    0.25215918 4.317354e-01
## SFARI ASD                  0.95180870 3.142967e-01
```

```
## FMRP Targets1              0.31184208 3.599767e-01
## FMRP Targets2              0.21524562 7.003694e-02
## CHD8 Targets1              0.03346473 5.806758e-02
## CHD8 Targets2              0.06733423 2.272613e-02
```

```
# FDR
```

```
FDRmat
```

```
##                      Non-Zero Modules Zero Modules
## Song Bird DE               0.8558001 0.0192105875
## Human-Specific1            0.6556139 0.5102327791
## Human-Specific2            0.9287687 0.5102327791
## ASD Prenatal1              0.7533912 0.6625555508
## ASD Prenatal2              0.7533912 0.7921408257
## ASD CTX Downreg            0.9937895 0.5102327791
## ASD CTX Upreg              0.7533912 0.0008120595
## ASD dnPTVs + pLI >= 0.9    0.6556139 0.5102327791
## SFARI ASD                  0.9937895 0.5102327791
## FMRP Targets1              0.6756578 0.5102327791
## FMRP Targets2              0.6556139 0.1820960499
## CHD8 Targets1              0.4350414 0.1820960499
## CHD8 Targets2              0.4376725 0.0984798866
```