Evaluation of Hubs, DCGs and DCLs on predicting AD with XGBoost

Gilderlanio Santana de Araújo

2023-03-20

```r
library("xgboost")
library("reshape2")
library("ggpubr")
```

```
## Loading required package: ggplot2
```

Initial considerations.

This script deals with pre-processing of gene expression data to investigate the predictive power in a classification study (Case x Control). XGBoost was implemented to verify the prediction regarding the following attibutes: differentially expressed genes, hubs identified in co-expression analyses, DCGs and DCLs identified in differential co-expression analyses.

To evaluate XGBoost, an AUC plot is generated with the average AUC obtained by cross-validation.

Pre-processing gene expression data

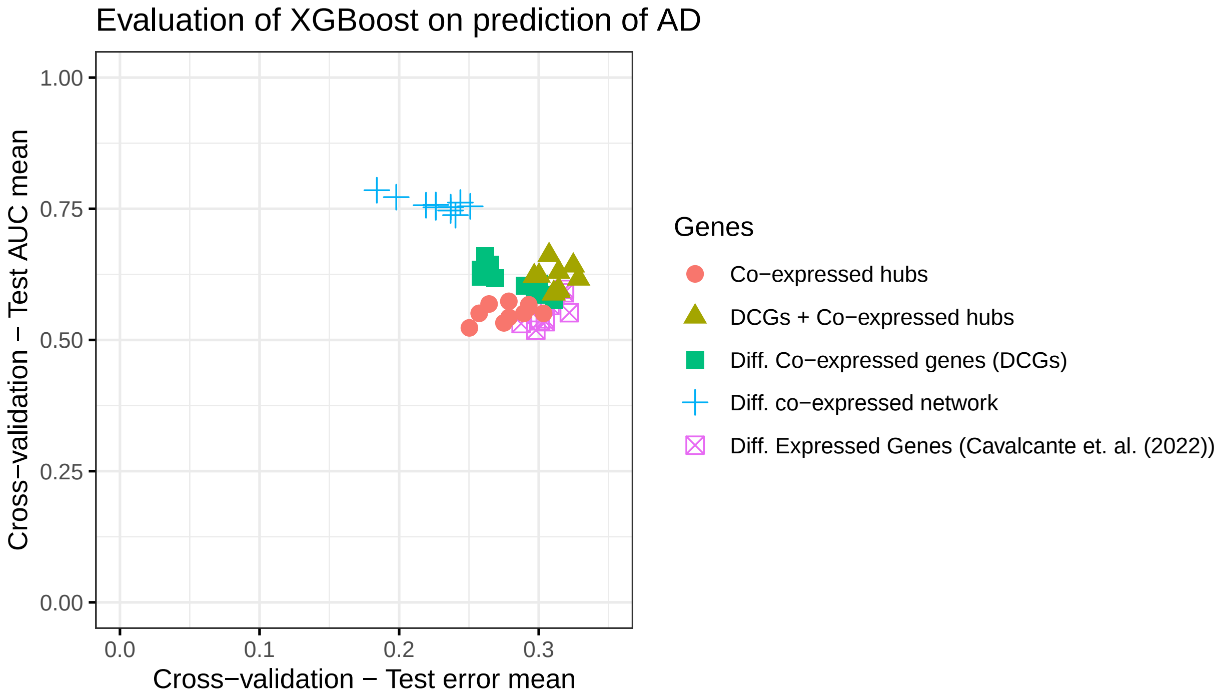
To add classes for each sample. Gene expression data must be randomized once the groups are in order. From 1 to 214 are AD cases and from 215 to 283 are control samples.

```r
# Annotation samples with classes (0 - Control, 1 - AD)

ad <- read.table("counts/AD_mat_GSE125583.txt", header = T, sep = "\t")
cn <- read.table("counts/cn_mat_GSE125583.txt", header = T, sep = "\t")
de <- read.table("results/DE.txt")
ad.f <- ad[rownames(ad) %in% de$V1,]
cn.f <- cn[rownames(cn) %in% de$V1,]

ad.f <- t(ad.f[order(rownames(ad.f)), ])
cn.f <- t(cn.f[order(rownames(cn.f)), ])
de <- rbind(ad.f, cn.f)

class.de <- rep(c(1, 0), c(219, 70))
de <- as.data.frame(de)
de$class <- class.de

de = de[sample(1:nrow(de)), ]
de = de[sample(1:nrow(de)), ]
de = de[sample(1:nrow(de)), ]

class.de <- de$class
de$class <- NULL

expression <- as.data.frame(t(read.table("counts/GSE125583_DiffCoexpInput.txt",
                                          header = T, sep = "\t")))
class <- rep(c(1, 0), c(214, 69))
expression$class <- class

# Shuffling samples (3x)

expression = expression[sample(1:nrow(expression)), ]
expression = expression[sample(1:nrow(expression)), ]
expression = expression[sample(1:nrow(expression)), ]

# getting classes after shuffling
class <- expression$class
expression$class <- NULL
```

```
# To extract gene expression for dcgs, hubs, and diffcoexp network

dcgs <- c("FAM153B", "CYP2C8", "CKMT1B")
hubs <- c("PKN2", "FNDC3A", "NRIP1", "TMTC2")
dcgs.hubs <- c("FAM153B", "CYP2C8", "CKMT1B", "PKN2", "FNDC3A", "NRIP1", "TMTC2")
dcls <- read.csv("results/DCL_GSE12.txt", sep = "\t")


all.genes <- Reduce(union, list(dcgs, hubs, dcls))

dcls <- union(dcls$Gene.1, dcls$Gene.2)
dcg.expression <- expression[, dcgs]
hub.expression <- expression[, hubs]
dcg.hub.expression <- expression[, dcgs.hubs]
net.expression <- expression[, dcls]

# To perform XBoost cross-validation for dcgs, hubs, and diffcoexp network

cv.de <- xgb.cv(data = as.matrix(de),
                 label = class.de, nrounds = 10,
                 nthread = 2, nfold = 5, metrics = list("rmse","auc", "error"),
                 max_depth = 2, eta = 1, objective = "binary:logistic", verbose = F)

cv.dcg <- xgb.cv(data = as.matrix(dcg.expression),
                 label = class, nrounds = 10,
                 nthread = 2, nfold = 5, metrics = list("rmse","auc", "error"),
                 max_depth = 2, eta = 1, objective = "binary:logistic", verbose = F)

cv.hub <- xgb.cv(data = as.matrix(hub.expression),
                 label = class, nrounds = 10,
                 nthread = 2, nfold = 5, metrics = list("rmse","auc", "error"),
                 max_depth = 2, eta = 1, objective = "binary:logistic", verbose = F)
```

```r
cv.dcg.hub <- xgb.cv(data = as.matrix(dcg.hub.expression),
                     label = class, nrounds = 10,
                     nthread = 2, nfold = 5, metrics = list("rmse","auc", "error"),
                     max_depth = 2, eta = 1, objective = "binary:logistic", verbose = F)

cv.net <- xgb.cv(data = as.matrix(net.expression),
                 label = class, nrounds = 10,
                 nthread = 2, nfold = 5, metrics = list("rmse","auc", "error"),
                 max_depth = 2, eta = 1, objective = "binary:logistic", verbose = F)

# To get raw evaluation results

cv.de.df <- as.data.frame(cv.de$evaluation_log)
cv.dcg.df <- as.data.frame(cv.dcg$evaluation_log)
cv.hub.df <- as.data.frame(cv.hub$evaluation_log)
cv.dcg.hub.df <- as.data.frame(cv.dcg.hub$evaluation_log)
cv.net.df <- as.data.frame(cv.net$evaluation_log)

# To annotate raw evaluation results

cv.de.df$Genes <- "Diff. Expressed Genes (Cavalcante et. al. (2022))"
cv.dcg.df$Genes <- "Diff. Co-expressed genes (DCGs)"
cv.hub.df$Genes <- "Co-expressed hubs"
cv.dcg.hub.df$Genes <- "DCGs + Co-expressed hubs"
cv.net.df$Genes <- "Diff. co-expressed network"

cv.all <- Reduce(rbind, list(cv.de.df, cv.dcg.df, cv.hub.df, cv.dcg.hub.df, cv.net.df))

# To extract error mean and AUC mean

cv.all.target <- cv.all[, c("test_auc_mean", "test_error_mean", "Genes", "iter")]
cv.all.target <- melt(cv.all.target, id.vars = c("Genes", "iter"))
```

```r
# To plot AUC and error mean

p <- ggscatter(cv.all, x = "test_error_mean",
          y = "test_auc_mean", color = "Genes",
          ggtheme = theme_bw(), shape = "Genes", size = 3,
          ylab = "Cross-validation - Test AUC mean",
          title = "Evaluation of XGBoost on prediction of AD",
          xlab = "Cross-validation - Test error mean")
ggpar(p, xlim =c(0.0, 0.35), ylim=c(0, 1))
```



```
gwas.file = "gwascatalog/gwas_catalog_v1.0-associations_e109_r2023-03-03.txt"
gwas.catalog <- read.csv(gwas.file, sep = "\t", header = F)
gwas.catalog <- na.omit(gwas.catalog)
gwas.catalog <- gwas.catalog[gwas.catalog$V7 %in% all.genes,]
gwas.catalog <- gwas.catalog[gwas.catalog$V10 <= 1e-8,]
gwas.catalog <- gwas.catalog[gwas.catalog$V9 != "?",]
write.table(gwas.catalog, file = "gwascatalog/OverlapDiffCoexpGwasCatalog.txt",
            sep = "\t", row.names = F, col.names = F, quote = F)
```