

Classification of Cancer Patients with Penalized Robust Nonconvex Loss Functions

Zhu Wang

University of Tennessee Health Science Center
zwang145@uthsc.edu

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This document presents analysis for the MAQC-II project, human breast cancer data set with penalized classification algorithms developed in Wang (2021) and implemented in R package `mpath`.

Dataset comes from the MicroArray Quality Control (MAQC) II project and includes 278 breast cancer samples with 164 estrogen receptor (ER) positive cases. The data files `GSE20194_series_matrix.txt.gz` and `GSE20194_MDACC_Sample_Info.xls` can be downloaded from <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?token=rhojvaiwkcsaihq&acc=GSE20194>. After reading the data, some unused variables are removed. From 22283 genes, the dataset is pre-screened to obtain 3000 genes with the largest absolute values of the two-sample t-statistics. The 3000 genes are standardized.

```
# The data files below were downloaded on June 1, 2016
require("openxlsx")
library("mpath")
bc <- t(read.delim("GSE20194_series_matrix.txt.gz", sep = "",
  header = FALSE, skip = 80))
colnames(bc) <- bc[1, ]
bc <- bc[-1, -c(1, 2)]
### The last column is empty with variable name
### !series_matrix_table_end, thus omitted
bc <- bc[, -22284]
mode(bc) <- "numeric" ### convert character to numeric
dat1 <- openxlsx::openxlsx("GSE20194_MDACC_Sample_Info.xls",
  sheet = 1, header = TRUE)
y <- dat1$characteristics..ER_status
y <- ifelse(y == "P", 1, -1)
table(y)
res <- rep(NA, dim(bc)[2])
for (i in 1:dim(bc)[2]) res[i] <- abs(t.test(bc[, i] ~ y)$statistic)
### find 3000 largest absolute value of t-statistic
tmp <- order(res, decreasing = TRUE)[1:3000]
dat <- bc[, tmp]
### standardize variables
```

```
dat <- scale(dat)
```

Set up configuration parameters.

```
### number of replicates
nrun <- 100
### penalty type
penalty <- c("enet", "snet", "mnet")
### Smallest value for lambda, as a fraction of lambda.max,
### the smallest value for which all coefficients are zero
### except the intercept
ratio <- 0.25
type.path <- "nonactive"
nlam <- ifelse(type.path != "onestep", 30, 100)
### The training data is contaminated by randomly switching
### response variable labels at varying pre-specified
### proportions
per <- c(0, 0.05, 0.1, 0.15)
### what quantity is minimized for tuning parameter
### selection
tuning <- "error"
n.cores <- 5
### robust nonconvex loss function, rfamily type and
### logistic
type <- c("closs", "gloss", "qloss", "binomial")
### and corresponding labels
type1 <- c("Closs", "Gloss", "Qloss", "Logistic")
### and corresponding tuning parameter
s <- c(0.9, 1.01, 0.5)
mstop <- 50
plot.it <- TRUE
```

The training data contains randomly selected 50 samples with positive estrogen receptor status and 50 samples with negative estrogen receptor status, and the rest were designated as the test data. The training data is contaminated by randomly switching response variable labels at varying pre-specified proportions `per=0, 0.05, 0.1, 0.15`. This process is repeated `nrun=100` times. Robust non-convex loss functions include C-loss, G-loss and Q-loss, each with penalty LASSO, SCAD and MCP. The initial values are derived using the boosting package `bst` with `mstop=50` and `nu` provided below depending on loss function `type`. For SCAD and MCP penalty, a penalty tuning parameter `gam` is provided below. To select optimal penalization tuning parameters, we run five-fold cross-validation averaging classification errors. The classification errors and number of selected variables are tabularized and plotted with `plot.it=TRUE`. Finally, this script also contains results with penalized logistic regression using `glmreg`.

```
summary7 <- function(x) c(summary(x), sd = sd(x))
ptm <- proc.time()
```

```

for (k in (1:4)) {
  ### k controls family argument rfamily type (see above)
  if (type[k] == "gloss")
    nu <- 0.1 else nu <- 0.01
  for (j in (1:3)) {
    ### j controls argument penalty type (see above)
    gam <- ifelse(penalty[j] == "snet", 3.7, 12)
    err.m1 <- nvar.m1 <- errbest.m1 <- lambest.m1 <- matrix(NA,
      ncol = 4, nrow = nrun)
    nvarbest.m1 <- mstopcv.m1 <- matrix(NA, ncol = 4, nrow = nrun)
    colnames(err.m1) <- c("cont-0%", "cont-5%", "cont-10%",
      "cont-15%")
    colnames(mstopcv.m1) <- colnames(nvarbest.m1) <- colnames(err.m1)
    colnames(nvar.m1) <- colnames(err.m1)
    colnames(errbest.m1) <- colnames(err.m1)
    colnames(lambest.m1) <- colnames(err.m1)
    for (ii in 1:nrun) {
      set.seed(1000 + ii)
      trid <- c(sample(which(y == 1))[1:50], sample(which(y ==
        -1))[1:50])
      dtr <- dat[trid, ]
      dte <- dat[-trid, ]
      ytrold <- y[trid]
      yte <- y[-trid]
      ### number of patients/no. variables in
      ### training and test data
      dim(dtr)
      dim(dte)
      ### randomly contaminate data
      ntr <- length(trid)
      set.seed(1000 + ii)
      con <- sample(ntr)
      for (i in (1:4)) {
        ### i controls how many percentage of data
        ### contaminated, see argument per above
        ytr <- ytrold
        percon <- per[i]
        ### randomly flip labels of the samples in
        ### training set according to pre-defined
        ### contamination level
        if (percon > 0) {
          ji <- con[1:(percon * ntr)]
          ytr[ji] <- -ytrold[ji]
        }
        ### fit a model with nclreg for nonconvex
        ### loss or glmreg for logistic loss, and
        ### use cross-validation to select best
        ### penalization parameter
        if (type[k] %in% c("closs", "gloss", "qloss")) {

```

```

dat.m1 <- nclreg(x = dtr, y = ytr, s = s[k],
  iter = 100, rfamily = type[k], penalty = penalty[j],
  lambda.min.ratio = ratio, gamma = gam, mstop.init = mstop,
  nu.init = nu, type.path = type.path, decreasing = FALSE,
  type.init = "bst")
lambda <- dat.m1$lambda[1:nlam]
set.seed(1000 + ii)
cvm1 <- cv.nclreg(x = dtr, y = ytr, nfolds = 5,
  n.cores = n.cores, parallel = TRUE, s = s[k],
  lambda = lambda, rfamily = type[k], penalty = penalty[j],
  gamma = gam, type = tuning, plot.it = FALSE,
  type.init = dat.m1$type.init, mstop.init = dat.m1$mstop.init,
  nu.init = dat.m1$nu.init, type.path = type.path,
  decreasing = dat.m1$decreasing)
err1 <- predict(dat.m1, newdata = dte, newy = yte,
  type = "error")
} else {
  dat.m1 <- glmreg(x = dtr, y = (ytr + 1)/2,
    family = type[k], penalty = penalty[j], lambda.min.ratio = ratio,
    gamma = gam)
  set.seed(1000 + ii)
  cvm1 <- cv.glmreg(x = dtr, y = (ytr + 1)/2,
    nfolds = 5, n.cores = n.cores, parallel = TRUE,
    lambda = dat.m1$lambda, family = type[k],
    penalty = penalty[j], gamma = gam, plot.it = FALSE)
  err1 <- apply((yte > -1) != predict(dat.m1,
    newx = dte, type = "class"), 2, mean)
}
optmstop <- cvm1$lambda.which
err.m1[ii, i] <- err1[optmstop]
nonzero <- predict(dat.m1, which = optmstop,
  type = "nonzero")
if (ii == 1)
  varid <- names(nonzero) else varid <- intersect(varid, names(nonzero))
nvar.m1[ii, i] <- length(nonzero)
errbest.m1[ii, i] <- min(err1, na.rm = TRUE)
lambest.m1[ii, i] <- which.min(err1)
nvarbest.m1[ii, i] <- length(predict(dat.m1,
  which = which.min(err1), type = "nonzero"))
}
if (ii%nrnrun == 0) {
  if (type[k] %in% c("closs", "gloss", "qloss"))
    cat(paste("\nfamily ", type1[k], ", s=", s[k],
      sep = ""), "\n") else cat(paste("\nfamily ", type1[k], sep = ""),
    "\n")
  pentype <- switch(penalty[j], enet = "LASSO",
    mnet = "MCP", snet = "SCAD")
  cat("penalty=", pentype, "\n")
  if (penalty[j] %in% c("snet", "mnet"))

```

```

        cat("gamma=", gam, "\n")
        cat("common variables selected:", varid, "\n")
        cat("best misclassification error\n")
        print(round(apply(errbest.m1, 2, summary7), 4))
        cat("which lambda has best error\n")
        print(round(apply(lambest.m1, 2, summary7), 1))
        cat("number of variables selected with best error\n")
        print(round(apply(nvarbest.m1, 2, summary7),
            1))
        cat("CV based misclassification error\n")
        print(round(apply(err.m1, 2, summary7), 4))
        cat("number of variables selected by CV\n")
        print(round(apply(nvar.m1, 2, summary7), 1))
        if (plot.it) {
            par(mfrow = c(2, 1))
            boxplot(err.m1, main = "Misclassification error",
                subset = "", sub = paste(type1[k], "-", pentype,
                    sep = ""))
            boxplot(nvar.m1, main = "No. variables", subset = "",
                sub = paste(type1[k], "-", pentype, sep = ""))
        }
    }
}
}
print(proc.time() - ptm)

```

```

sessionInfo()
## R version 4.5.3 (2026-03-11)
## Platform: aarch64-apple-darwin25.3.0
## Running under: macOS Tahoe 26.5.2
##
## Matrix products: default
## BLAS:   /opt/homebrew/Cellar/openblas/0.3.31_1/lib/libopenblas-r0.3.31.dylib
## LAPACK: /opt/homebrew/Cellar/r/4.5.3/lib/R/lib/libRlapack.dylib; LAPACK version 3.12.1
##
## locale:
## [1] C.UTF-8/C.UTF-8/C.UTF-8/C/C.UTF-8/C.UTF-8
##
## time zone: America/Chicago
## tzcode source: internal
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets
## [6] methods    base
##
## other attached packages:
## [1] knitr_1.51

```

```
##  
## loaded via a namespace (and not attached):  
## [1] compiler_4.5.3 cli_3.6.6      formatR_1.14  
## [4] tools_4.5.3    ote1_0.2.0      xfun_0.56  
## [7] rlang_1.2.0    evaluate_1.0.5
```

References

Zhu Wang. Mm for penalized estimation. *TEST*, April 2021. URL <https://doi.org/10.1007/s11749-021-00770-2>.