

SIS NMF Final: Diagnosis to DSD

November 29, 2014

1 Preparation

```
##### LIBRARIES
options(java.parameters = "-Xmx4G")

library(survival)

## Loading required package: splines

library(energy)
library(NMF)

## Loading required package: methods
## Loading required package: pkgmaker
## Loading required package: registry
## Loading required package: rngtools
## Loading required package: cluster
## NMF - BioConductor layer [OK] | Shared memory capabilities [NO: bigmemory] | Cores 31/32
## To enable shared memory capabilities, try: install.extras('
## NMF
## ')

library(nnlsl)

library(glmulti)

## Loading required package: rJava
##
## Attaching package: 'glmulti'
##
## The following object is masked from 'package:NMF':
##
##   consensus

library(glmnet)

## Loading required package: Matrix
## Loaded glmnet 1.9-8

library(RColorBrewer)
library(gplots)

##
## Attaching package: 'gplots'
##
```

```
## The following object is masked from 'package:stats':
##
##      lowess

library(xtable)
library(stargazer)

##
## Please cite as:
##
## Hlavac, Marek (2014). stargazer: LaTeX code and ASCII text for well-formatted regression
and summary statistics tables.
## R package version 5.1. http://CRAN.R-project.org/package=stargazer

load("image.rda")
```

2 Probe selection

```
table(cpss.sis$sel)

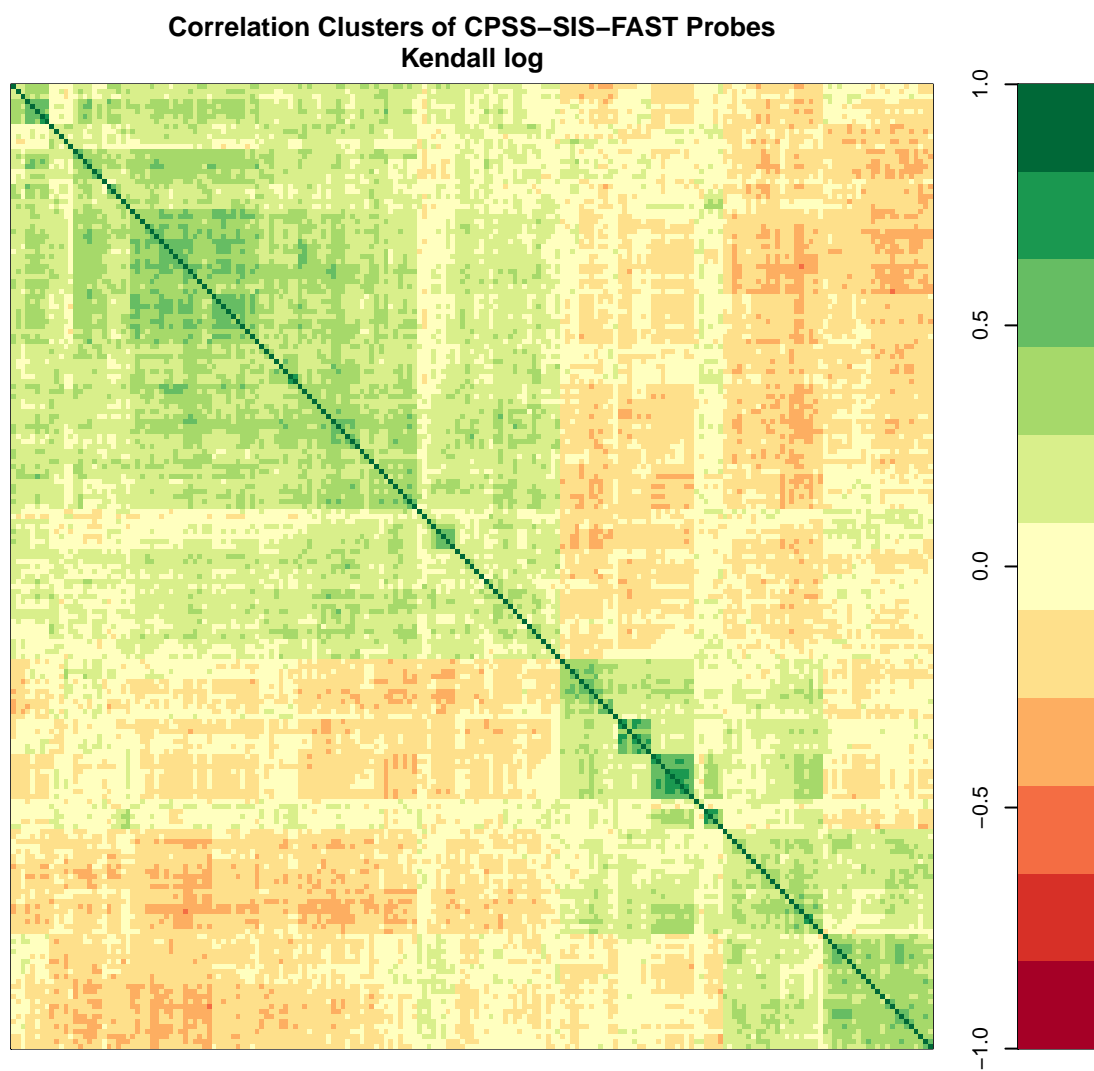
##
## FALSE  TRUE
## 12807   193

mean(cpss.sis$sel)

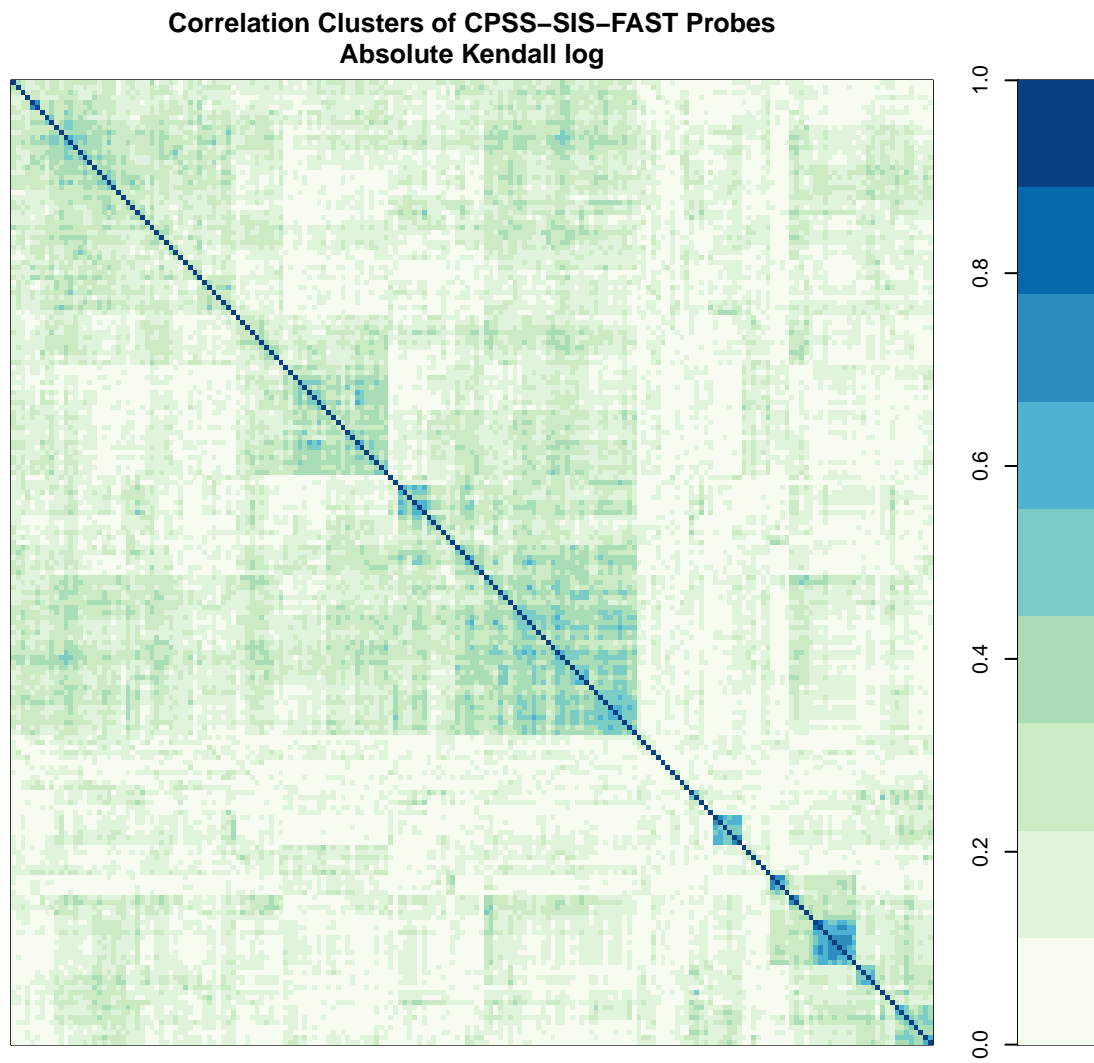
## [1] 0.01485
```

3 Expression correlation

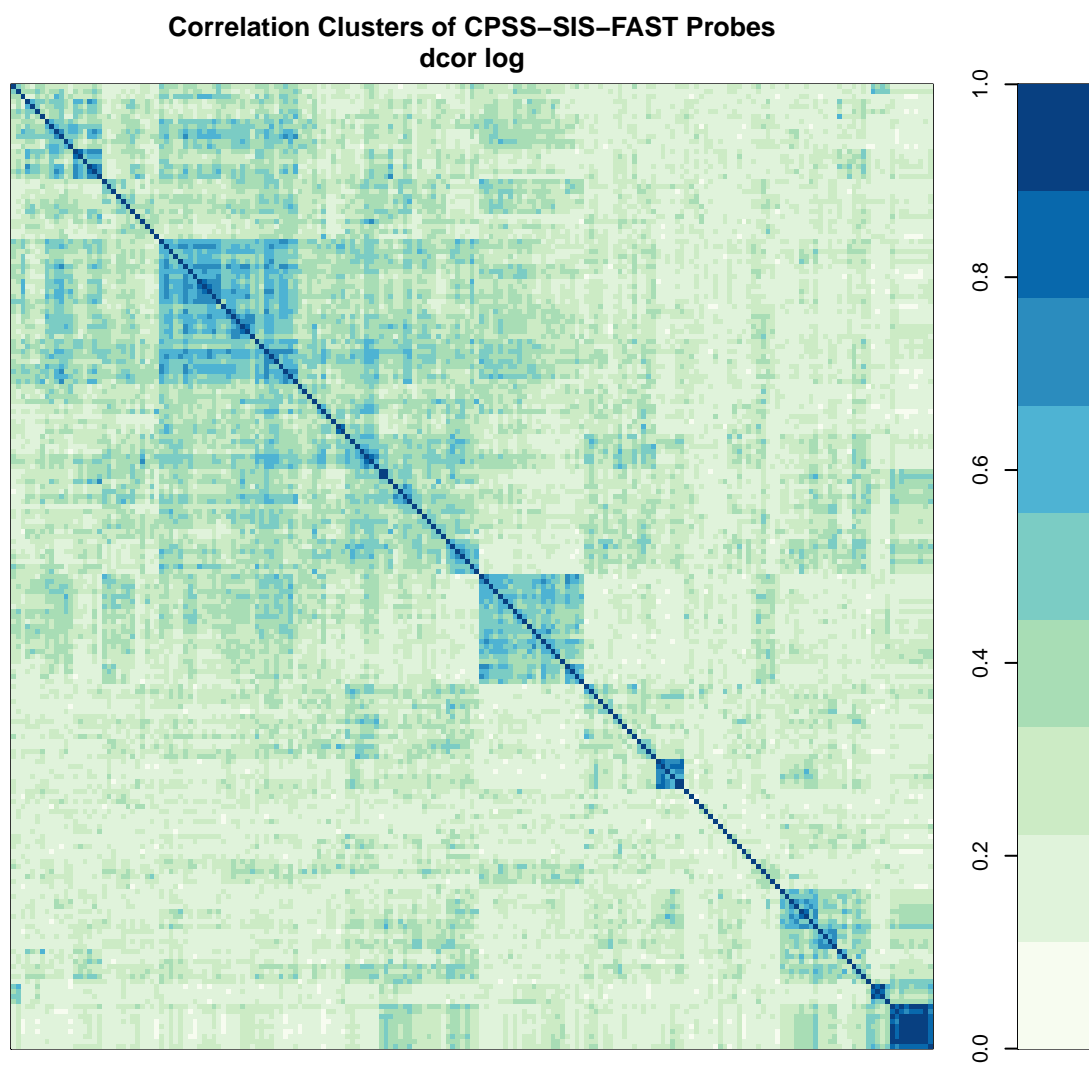
```
corPlot(x.sel.kcor, main = "Correlation Clusters of CPSS-SIS-FAST Probes\nKendall log",
        useRaster = FALSE)
```



```
corPlot(abs(x.sel.kcor), zlim = c(0, 1), pal = "GnBu", main = "Correlation Clusters of CPSS–SIS–FAST Probes",
        useRaster = FALSE)
```

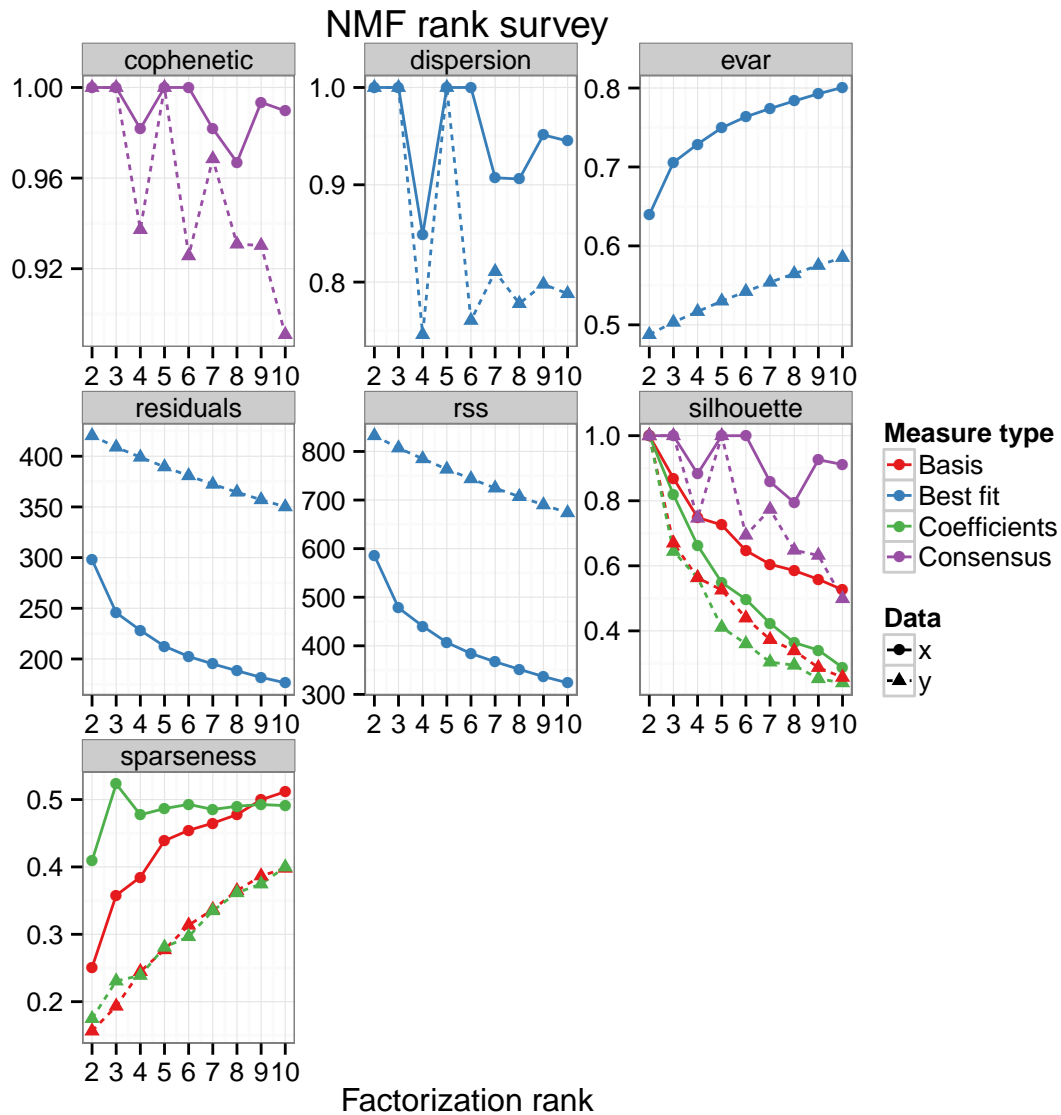


```
corPlot(x.sel.dcor, zlim = c(0, 1), pal = "GnBu", main = "Correlation Clusters of CPSS-SIS-FAST Probes",
        useRaster = FALSE)
```



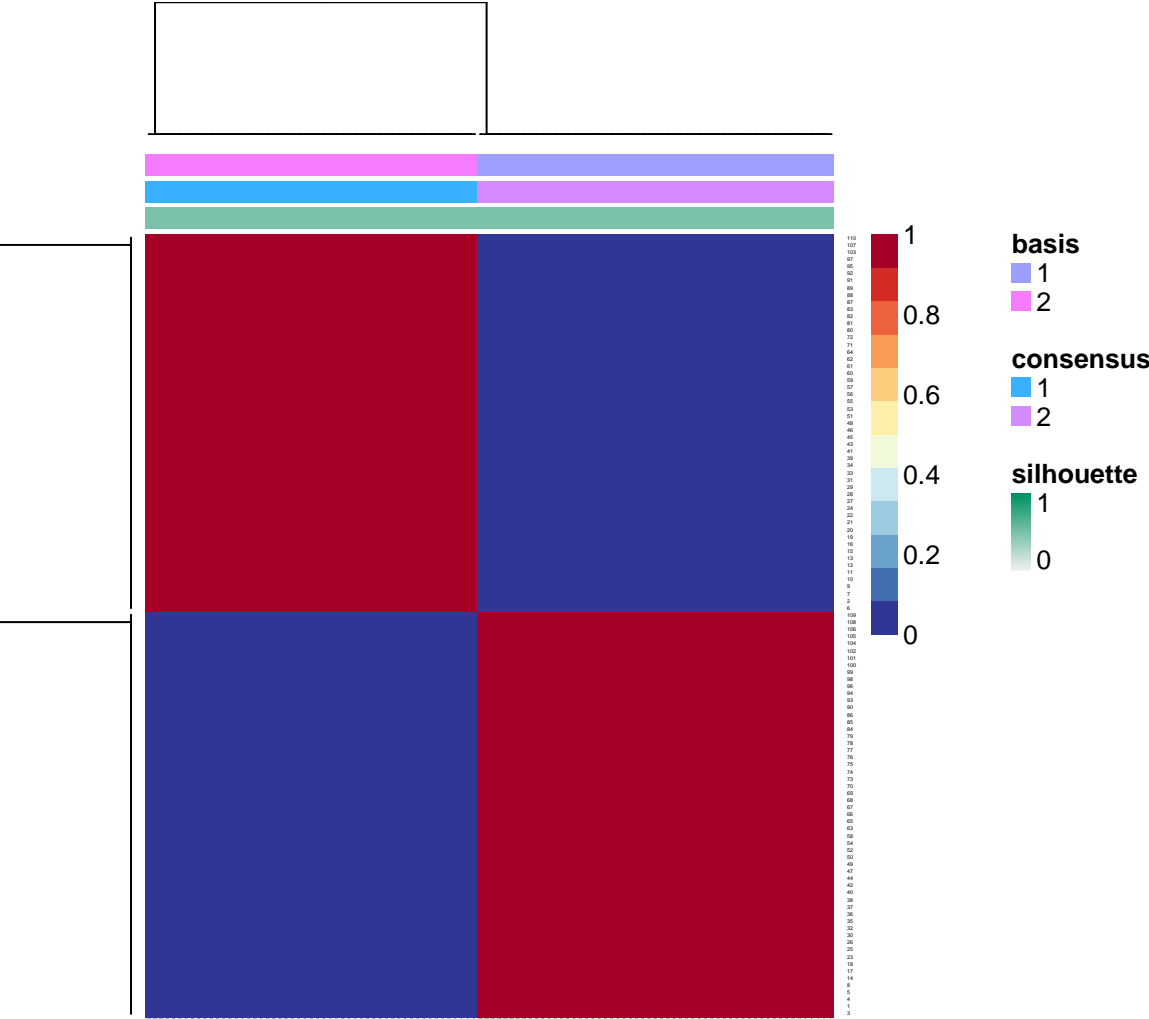
4 Factorization

```
plot(nmf.runs.rank, nmf.runs.rank.random[[1]])
```

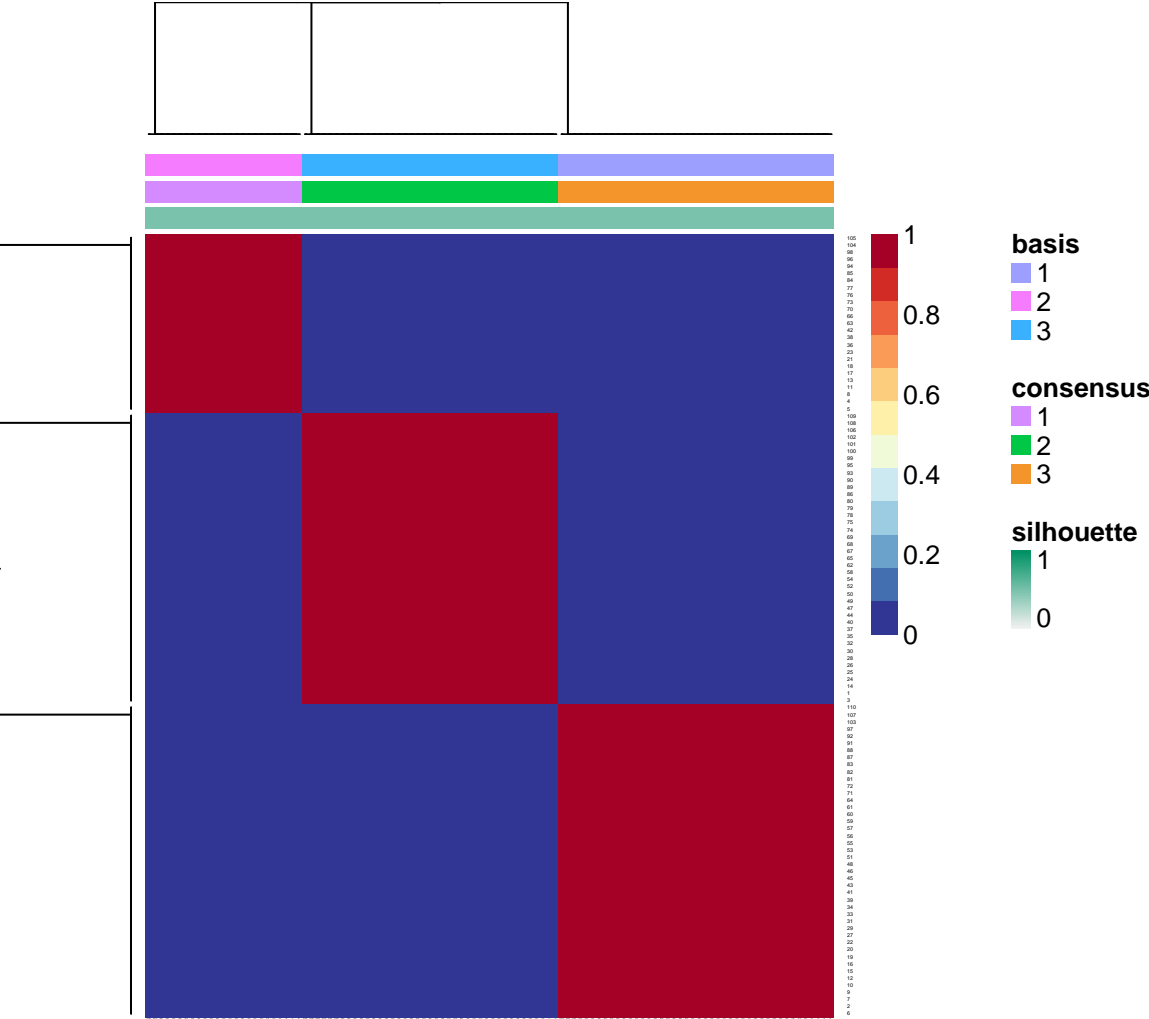


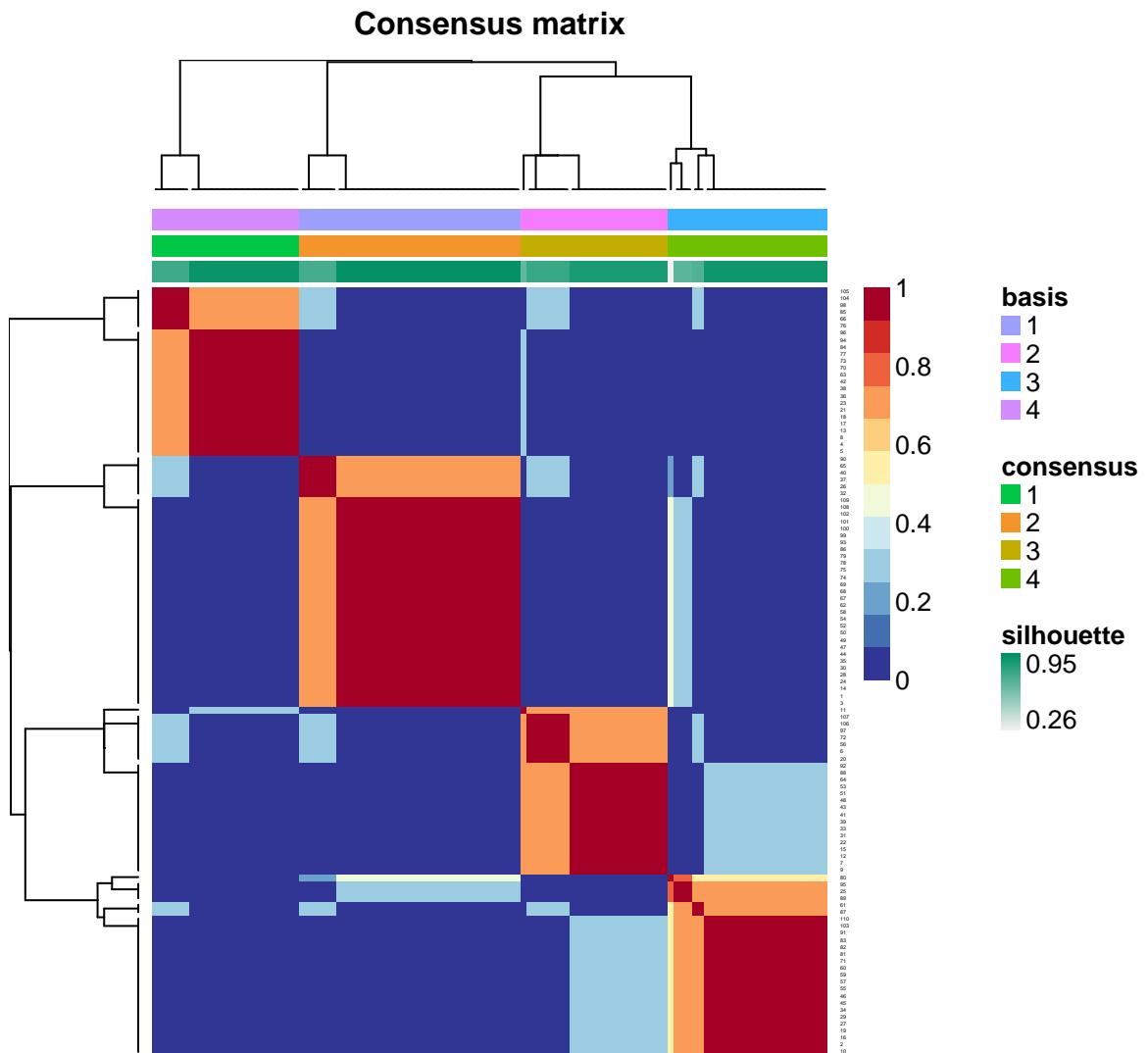
```
for (i in nmf.runs.rank$fit) {
  consensusmap(i)
}
```

Consensus matrix

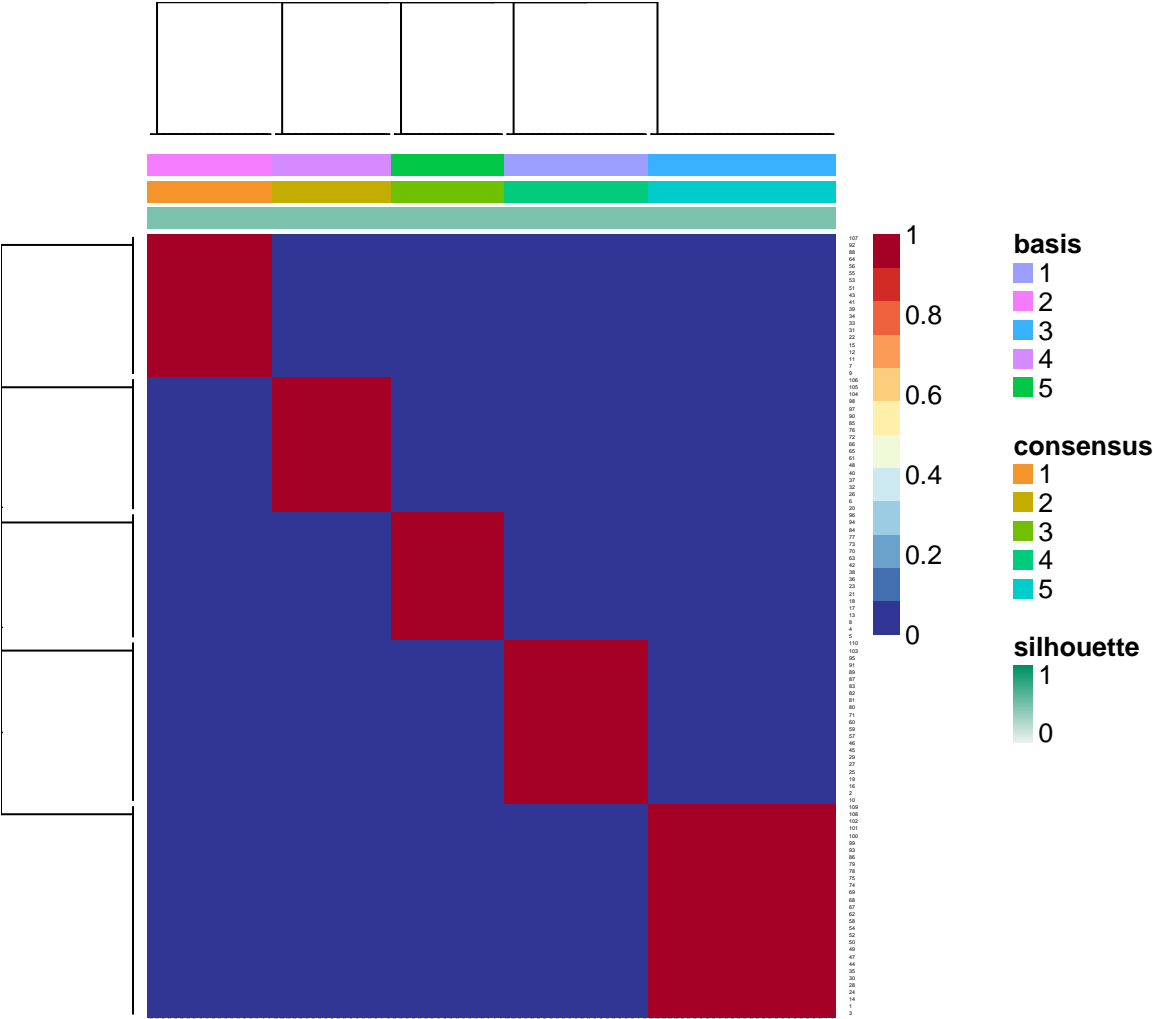


Consensus matrix

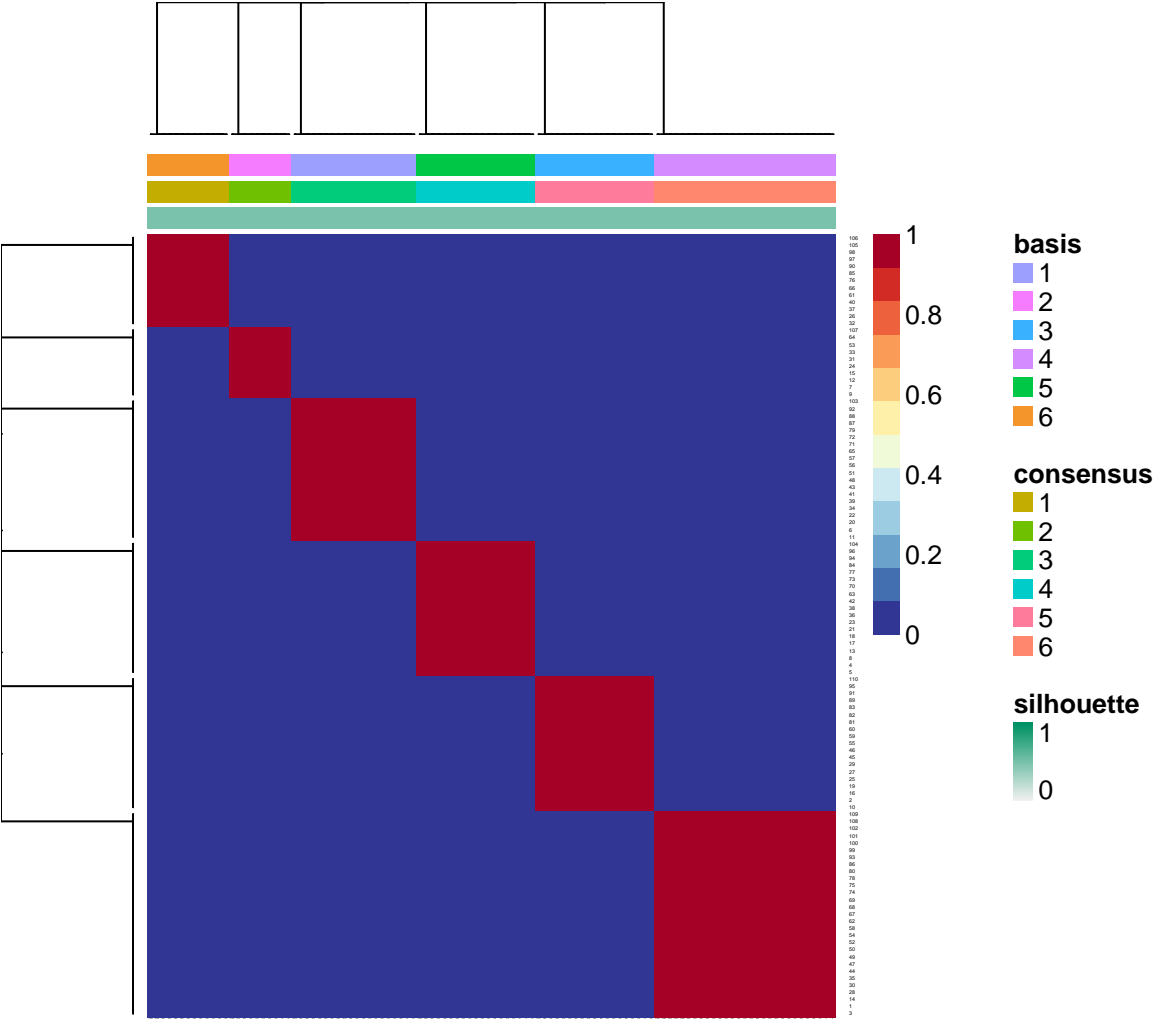


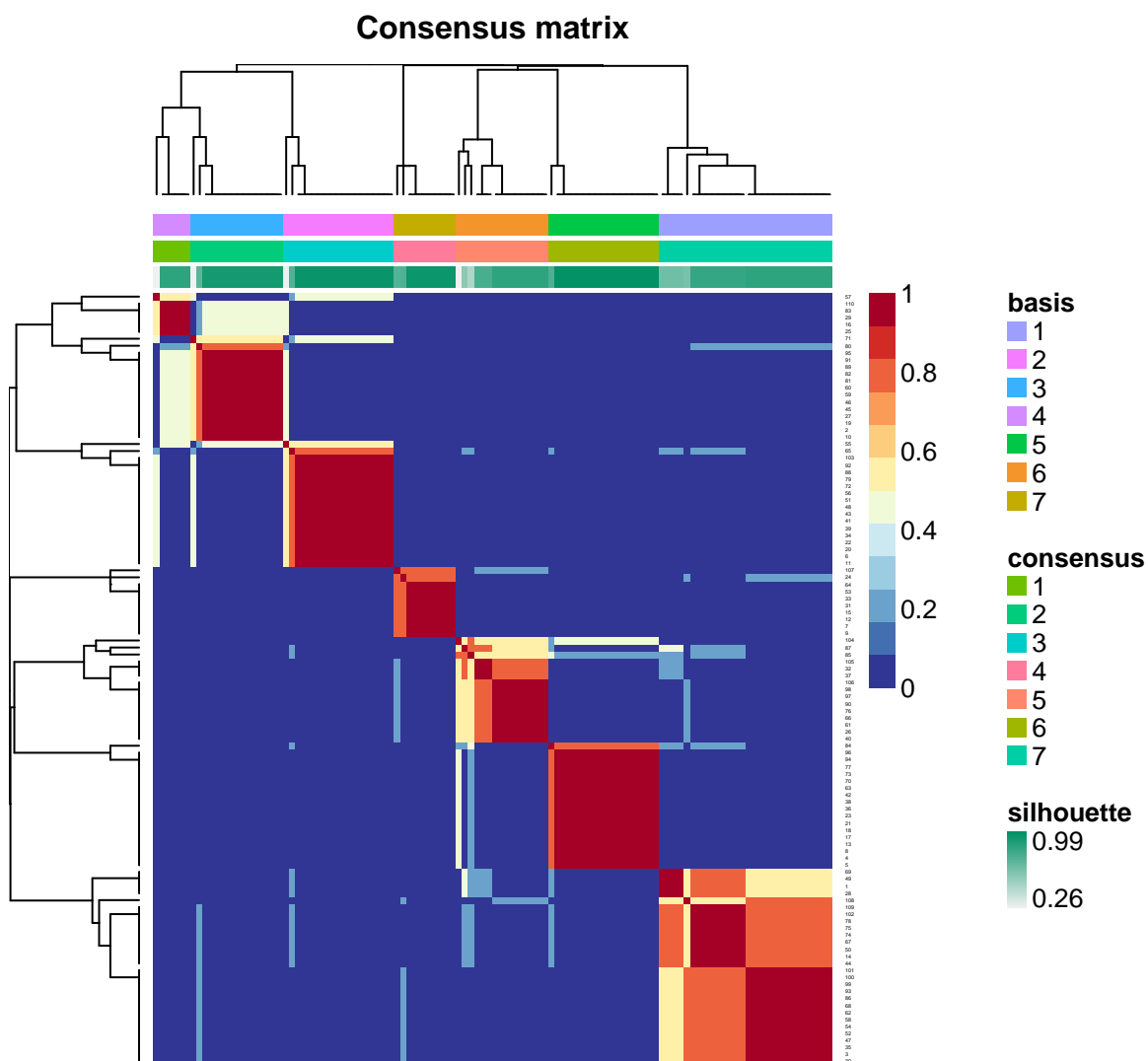


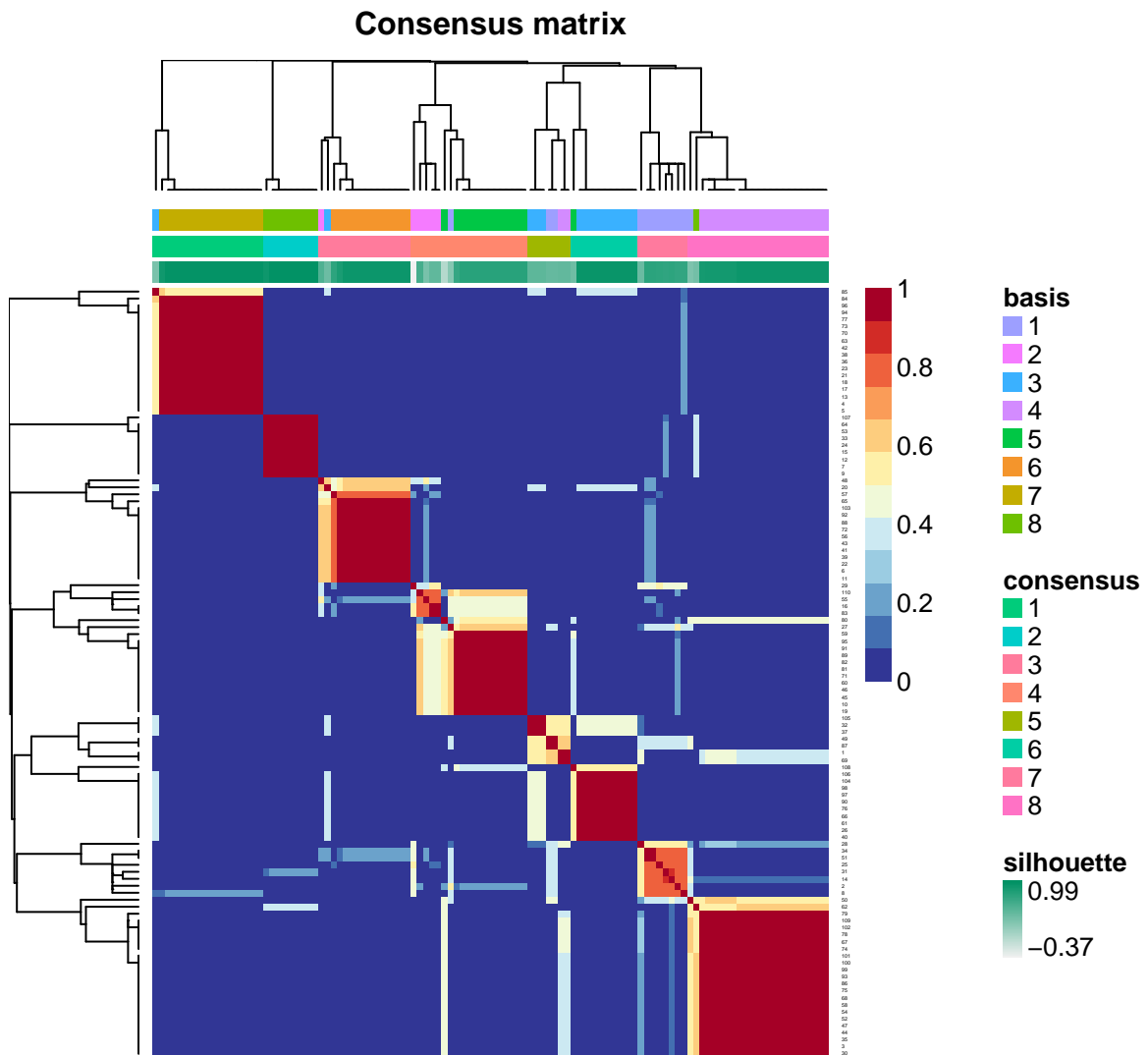
Consensus matrix

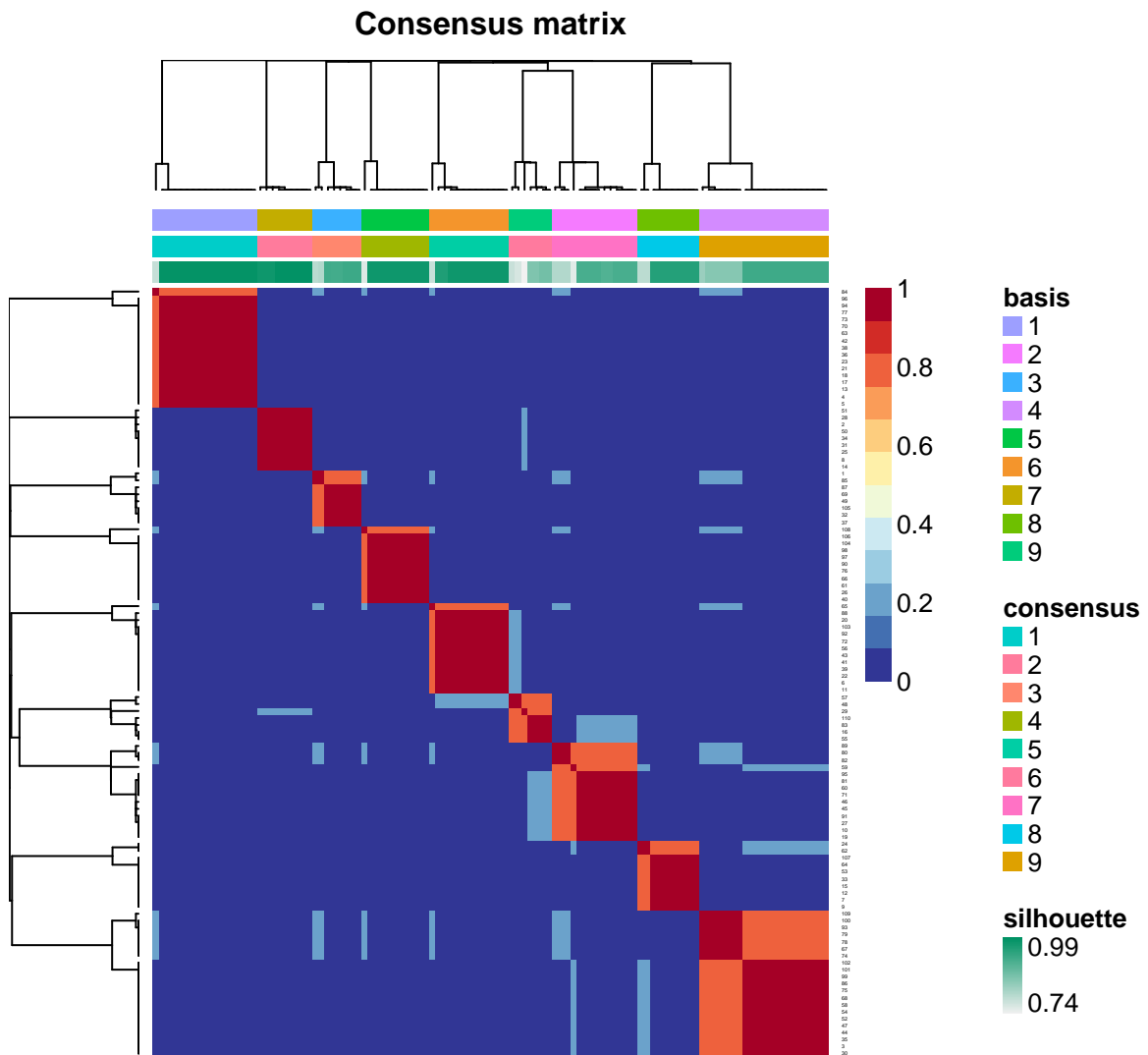


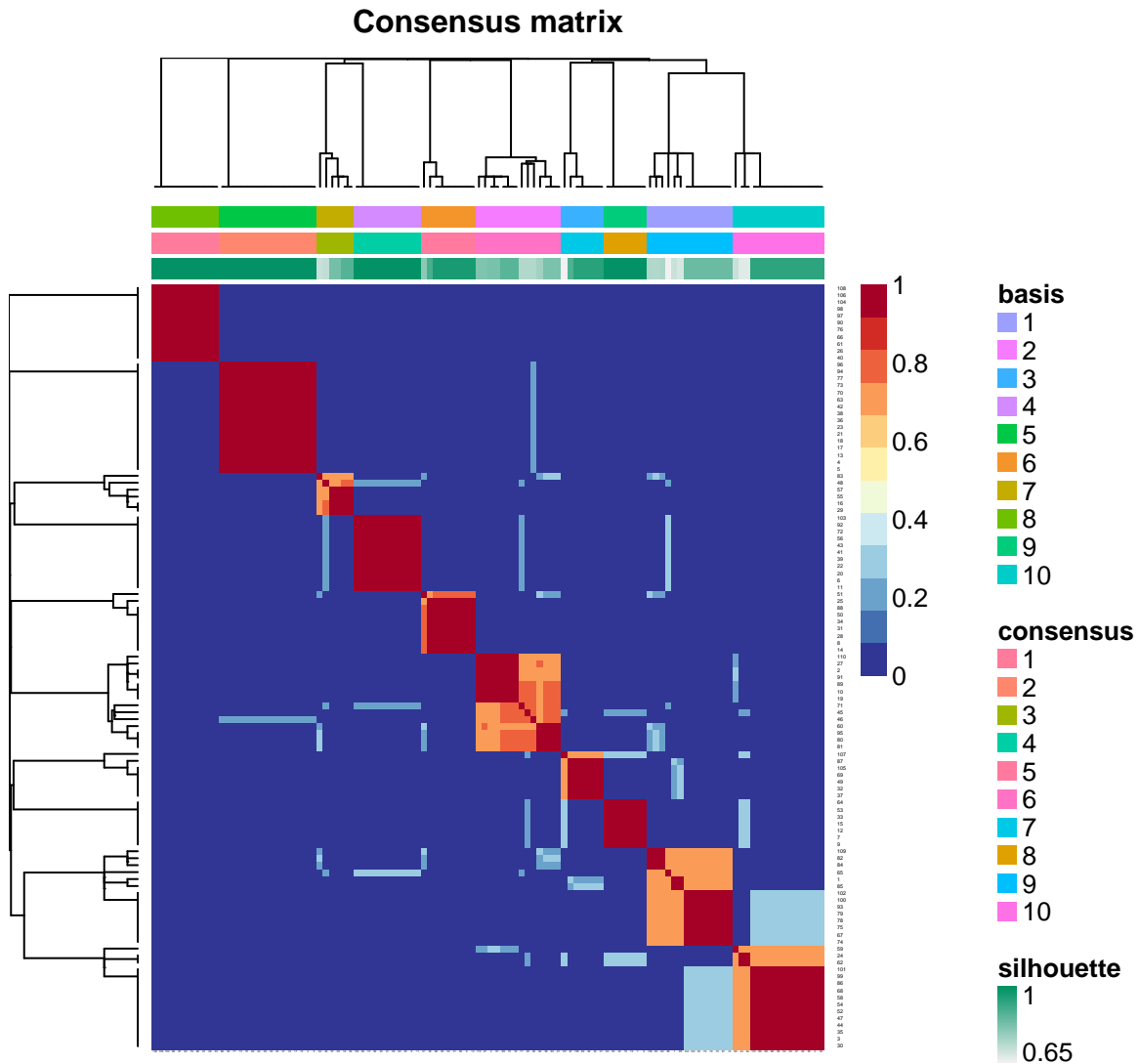
Consensus matrix











```

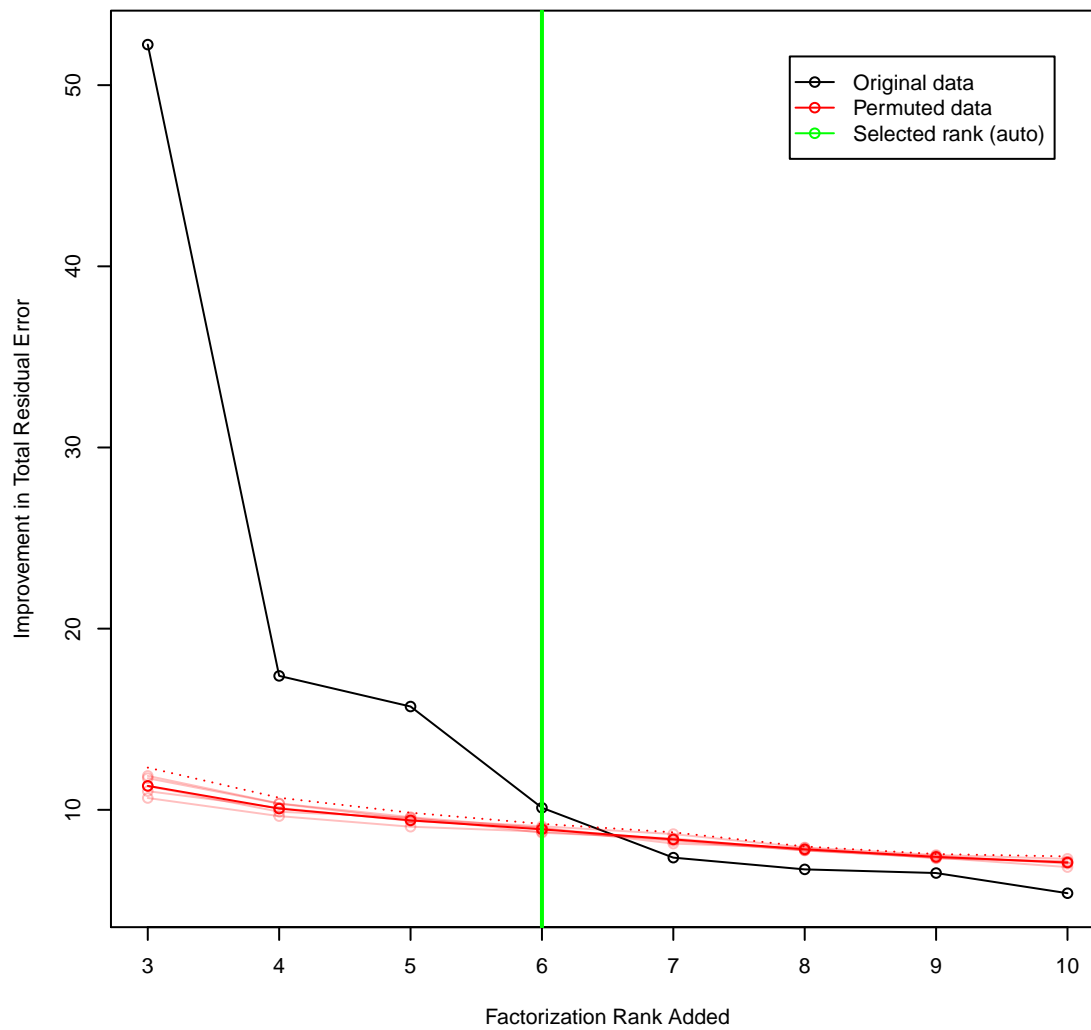
plot(nmf.rankrange[-1], -temp.orig_resids.delta, type = "o", col = "black",
     pch = 21, ylim = range(-c(temp.orig_resids.delta, temp.perm_resids.delta.mean)),
     xlab = "Factorization Rank Added", ylab = "Improvement in Total Residual Error")
lines(nmf.rankrange[-1], -temp.perm_resids.delta.mean, col = "red", type = "o",
      pch = 21, lwd = 1)
for (i in 1:ncol(temp.perm_resids)) {
  lines(nmf.rankrange[-1], -temp.perm_resids.delta[, i], type = "o", col = rgb(1,
    0, 0, 0.25))
}
lines(nmf.rankrange[-1], -temp.perm_resids.delta.threshold, col = "red", lty = "dotted")
if (nmf.rank.wasauto == TRUE) {
  temp.col = "green"
} else {
  temp.col = "blue"
}
abline(v = nmf.rank, col = temp.col, lwd = 2)
legend("topright", legend = c("Original data", "Permuted data", sprintf("Selected rank (%s)",

```

```

ifelse(nmf.rank.wasauto == TRUE, "auto", "fixed")), col = c("black", "red",
temp.col), lty = "solid", pch = 21, inset = 0.05)

```

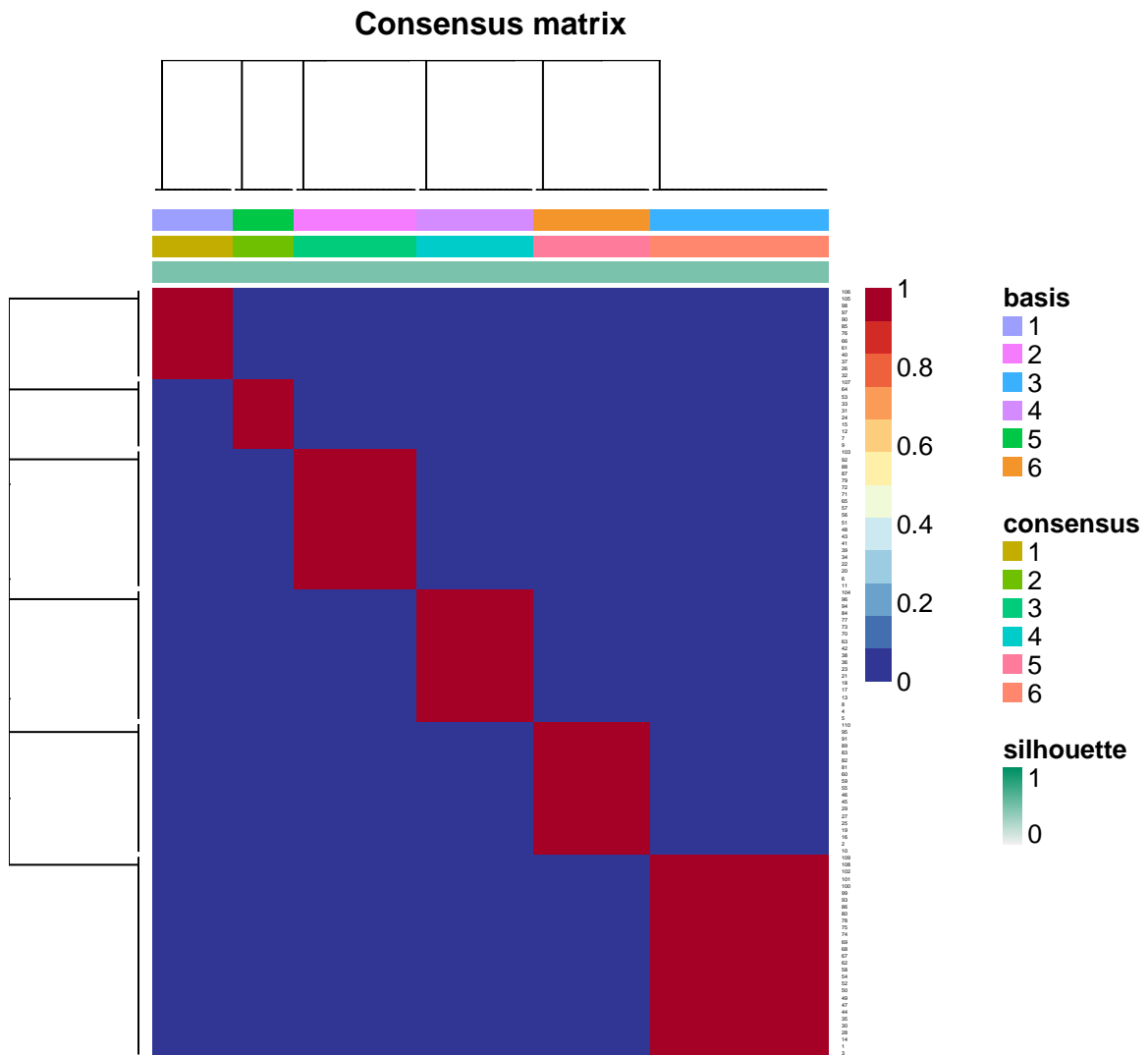


4.1 Fit

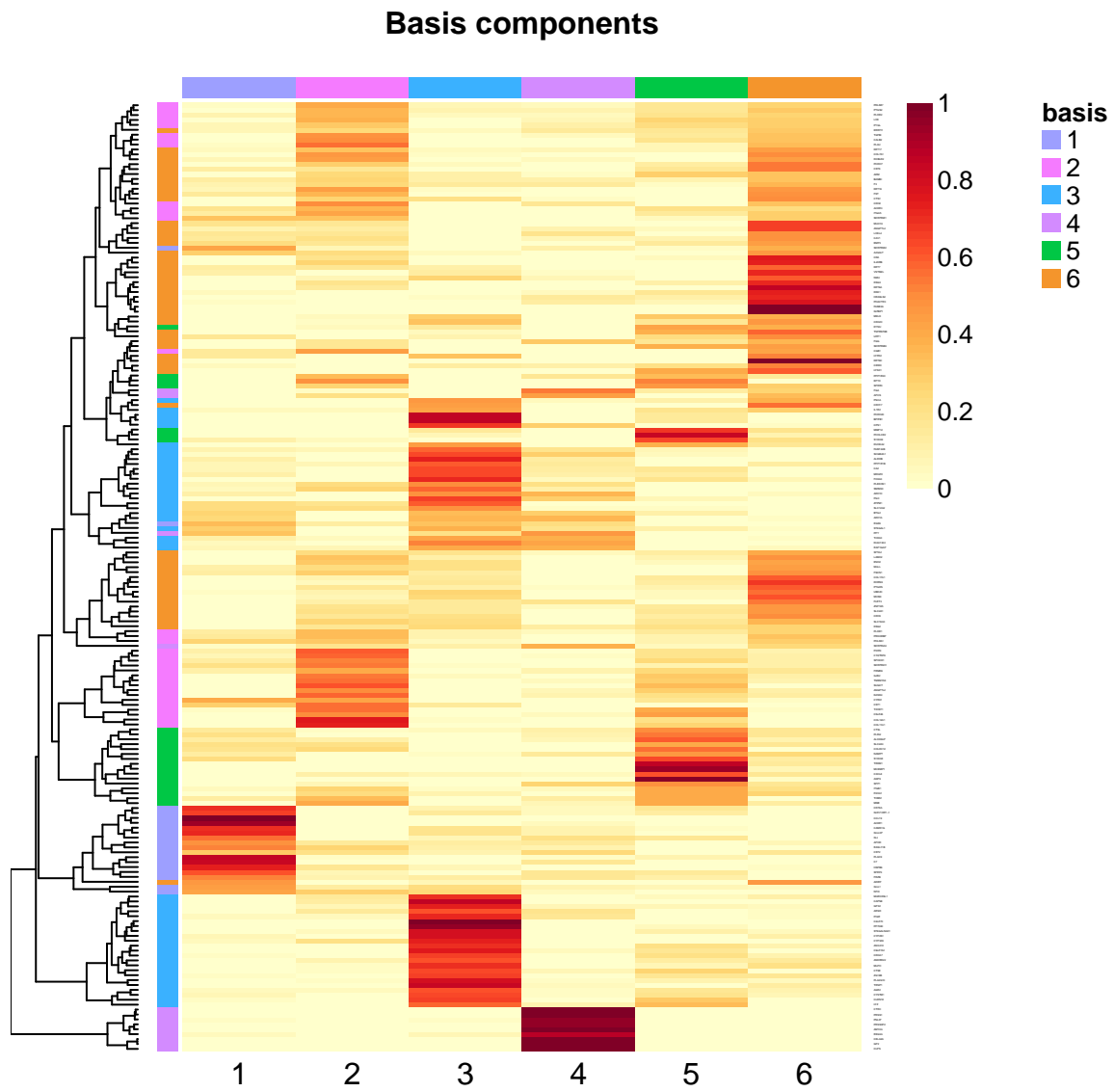
```

consensusmap(nmf.final)

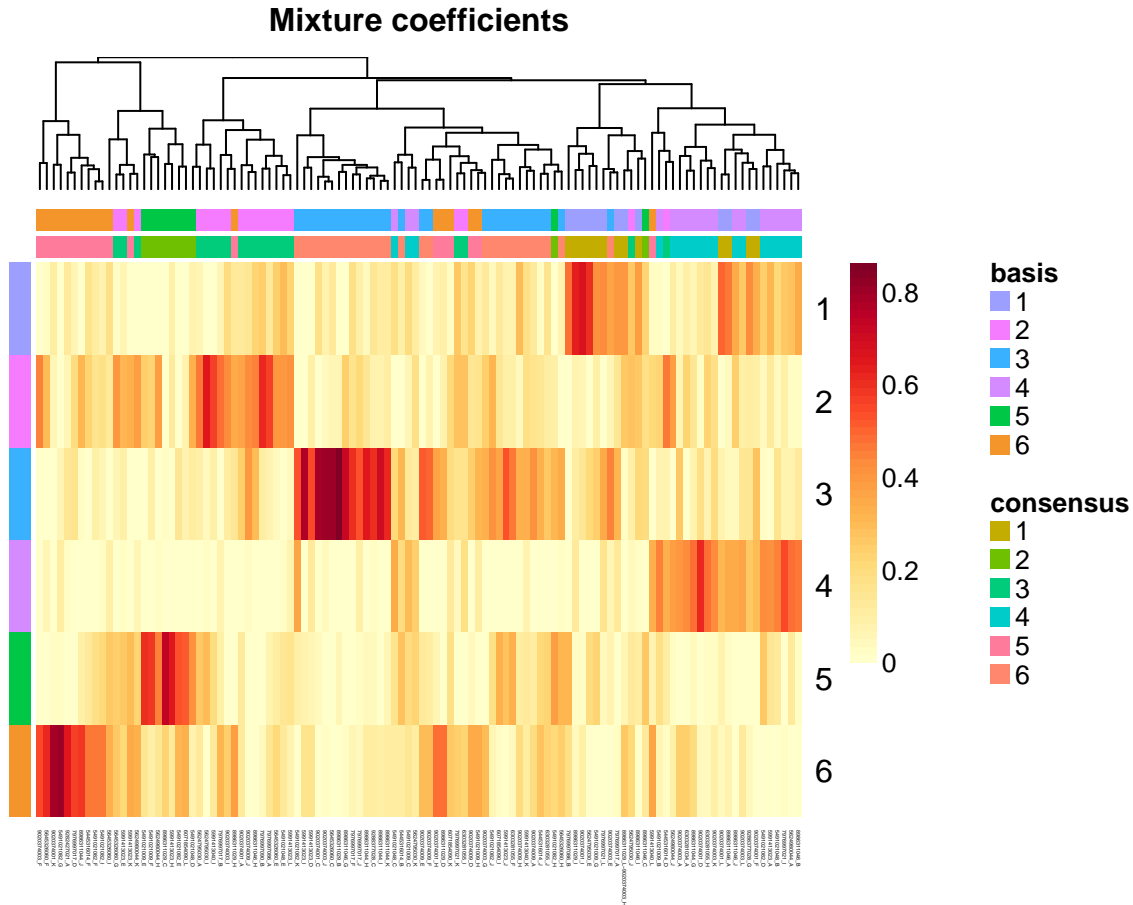
```

```
basimap(nmf.final)
```



```
coefmap(nmf.final)
```



```

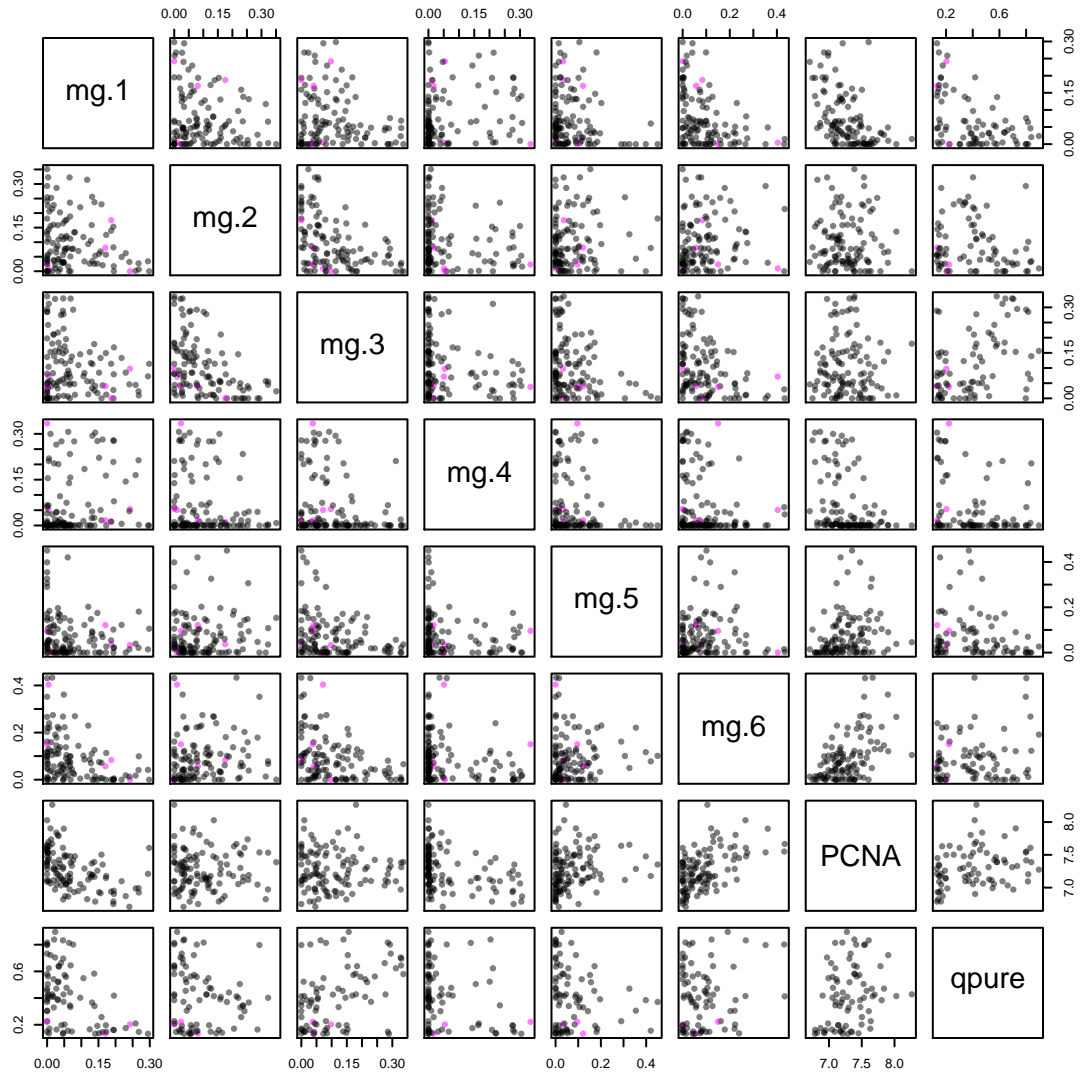
coefs.diag_dsd = apply(xlin.diag_dsd.sel, 2, function(xcol) nnls(basis(nmf.final),
  xcol)$x)
coefs.diag_rec = apply(xlin.diag_rec.sel, 2, function(xcol) nnls(basis(nmf.final),
  xcol)$x)
coefs.recr_dsd = apply(xlin.recr_dsd.sel, 2, function(xcol) nnls(basis(nmf.final),
  xcol)$x)
coefs.pdac_au = apply(xlin.pdac_au.sel, 2, function(xcol) nnls(basis(nmf.final),
  xcol)$x)

```

```

temp.pred.pairs = t(rbind(coefs.pdac_au, metapcna.scores[colnames(coefs.pdac_au)]))
colnames(temp.pred.pairs) = paste("mg", 1:ncol(temp.pred.pairs), sep = ".")
colnames(temp.pred.pairs)[ncol(temp.pred.pairs)] = "PCNA"
temp.pred.pairs = cbind(temp.pred.pairs, qpure = samp.pdac_au$purity_qpure)
pairs(temp.pred.pairs, pch = 16, cex = 1, col = ifelse(rownames(temp.pred.pairs) %in%
  colnames(xlin.diag_dsd.sel), rgb(0, 0, 0, 0.5), rgb(1, 0, 1, 0.5)))

```



4.2 Prediction on training set

```
nmf.final.cpv.pvals = data.frame(surv.diag_rec.p = apply(coefs.diag_rec, 1,
function(xc) pchisq(2 * diff(coxph(y.diag_rec ~ xc)$loglik), df = 1, lower.tail = FALSE)),
surv.diag_rec.c = apply(coefs.diag_rec, 1, function(xc) coef(coxph(y.diag_rec ~
xc))), surv.diag_dsd.p = apply(coefs.diag_dsd, 1, function(xc) pchisq(2 *
diff(coxph(y.diag_dsd ~ xc)$loglik), df = 1, lower.tail = FALSE)), surv.diag_dsd.c = apply(coefs
1, function(xc) coef(coxph(y.diag_dsd ~ xc))), surv.recr_dsd.p = apply(coefs.recr_dsd,
1, function(xc) pchisq(2 * diff(coxph(y.recr_dsd ~ xc)$loglik), df = 1,
lower.tail = FALSE)), surv.recr_dsd.c = apply(coefs.recr_dsd, 1,
function(xc) coef(coxph(y.recr_dsd ~ xc))), pure.p = apply(coefs.pdac_au,
1, function(xc) cor.test(samps.pdac_au$purity_qpure, xc, method = "kendall")$p.value),
pure.s = apply(coefs.pdac_au, 1, function(xc) cor.test(samps.pdac_au$purity_qpure,
xc, method = "kendall")$statistic))
temp.pvals = as.matrix(nmf.final.cpv.pvals[, grepl("\\.p$", colnames(nmf.final.cpv.pvals))])
```

```
temp.pvals.FWER = matrix(p.adjust(as.vector(temp.pvals), "holm"), nrow = nrow(temp.pvals))
colnames(temp.pvals.FWER) = paste(colnames(temp.pvals), "Holm", sep = ".")
temp.pvals.BY = matrix(p.adjust(as.vector(temp.pvals), "BY"), nrow = nrow(temp.pvals))
colnames(temp.pvals.BY) = paste(colnames(temp.pvals), "BY", sep = ".")
nmf.final.cpv.pvals = cbind(nmf.final.cpv.pvals, temp.pvals.FWER, temp.pvals.BY)
nmf.final.cpv.pvals = nmf.final.cpv.pvals[, order(colnames(nmf.final.cpv.pvals))]
```

	pure.p	pure.p.BY	pure.p.Holm	pure.s	surv.diag_dsd.c	surv.diag_dsd.p	surv.diag_dsd.p.BY	surv.diag_dsd.p.Holm	surv.diag_rec.c	surv.diag_rec.p	surv.diag_rec.p.BY	surv.diag_rec.p.Holm	surv.rec_dsd.c	surv.rec_dsd.p	surv.rec_dsd.p.BY	surv.rec_dsd.p.Holm
1	0.00	0.01	0.01	-3.42	-4.56	0.00	0.04	0.06	-3.78	0.01	0.07	0.11	-2.36	0.16	0.75	0.96
2	0.05	0.30	0.50	-1.96	3.10	0.02	0.15	0.25	1.99	0.11	0.55	0.77	2.62	0.06	0.35	0.56
3	0.00	0.00	0.00	3.91	-5.46	0.00	0.00	0.00	-2.64	0.03	0.19	0.33	-4.66	0.00	0.04	0.04
4	0.03	0.19	0.33	-2.19	-0.95	0.44	1.00	1.00	-1.68	0.16	0.75	0.96	0.56	0.68	1.00	1.00
5	0.07	0.38	0.57	-1.81	2.84	0.02	0.12	0.21	2.73	0.01	0.12	0.20	1.37	0.29	1.00	1.00
6	0.78	1.00	1.00	0.28	6.61	0.00	0.00	0.00	5.49	0.00	0.00	0.00	3.97	0.00	0.04	0.06

Table 1: Resubstitution prediction, all tests

	pure.p.Holm	pure.s	surv.diag_dsd.c	surv.diag_dsd.p.Holm	surv.diag_rec.c	surv.diag_rec.p.Holm	surv.rec_dsd.c	surv.rec_dsd.p.Holm
1	0.01	-3.42	-4.56	0.06	-3.78	0.11	-2.36	0.96
2	0.50	-1.96	3.10	0.25	1.99	0.77	2.62	0.56
3	0.00	3.91	-5.46	0.00	-2.64	0.33	-4.66	0.04
4	0.33	-2.19	-0.95	1.00	-1.68	0.96	0.56	1.00
5	0.57	-1.81	2.84	0.21	2.73	0.20	1.37	1.00
6	1.00	0.28	6.61	0.00	5.49	0.00	3.97	0.06

Table 2: Resubstitution prediction, Holm MTC only

MTC P-values

```
print(asreg.result)
```

```
## glmulti.analysis
## Method: h / Fitting: coxph / IC used: bic
## Level: 2 / Marginality: TRUE
## From 100 models:
## Best IC: 551.558245978867
## Best model:
## [1] "Surv(time, event) ~ 1 + mg.5 + mg.6"
## Evidence weight: 0.121525761025609
## Worst IC: 561.093163081812
## 5 models within 2 IC units.
## 71 models to reach 95% of evidence weight.
```

```
coef(asreg.result)
```

```
##          Estimate Uncond. variance Nb models Importance +/- (alpha=0.05)
## mg.1:mg.4 -0.00342      0.001098         1    0.001595      0.06569
## mg.2:mg.4  0.06847      0.024924         2    0.003030      0.31297
## mg.4:mg.5 -0.05064      0.019737         1    0.003679      0.27850
## mg.4:mg.6  0.02227      0.015093         2    0.004699      0.24355
## mg.2:mg.3  0.08587      0.057059         3    0.004885      0.47354
## mg.1:mg.2  0.10761      0.069012         2    0.004997      0.52078
## mg.1:mg.5 -0.01322      0.015809         2    0.005116      0.24925
## mg.3:mg.4 -0.25668      0.347670         4    0.008845      1.16890
## mg.3:mg.5  0.01013      0.047858         3    0.009870      0.43368
## mg.2:mg.5  0.09367      0.064793         4    0.010069      0.50461
```

```
## mg.5:mg.6  0.10404      0.413552      8  0.036678      1.27485
## mg.1:mg.6  0.75549      3.893974      8  0.039107      3.91192
## mg.1:mg.3 -1.05886      7.166918      9  0.043683      5.30712
## mg.2:mg.6 -1.53508      9.333667     13  0.074749      6.05646
## mg.3:mg.6  2.60281     29.616218     14  0.097762     10.78842
## mg.4       0.09036      0.113089     33  0.136430      0.66666
## mg.2       0.33327      0.778397     42  0.219557      1.74902
## mg.1      -1.85625      6.374836     54  0.439670      5.00527
## mg.5       1.08749      2.127350     49  0.444550      2.89143
## mg.3      -2.66620      7.511723     65  0.592820      5.43329
## mg.6       5.31298      5.463222     90  0.932557      4.63359
```

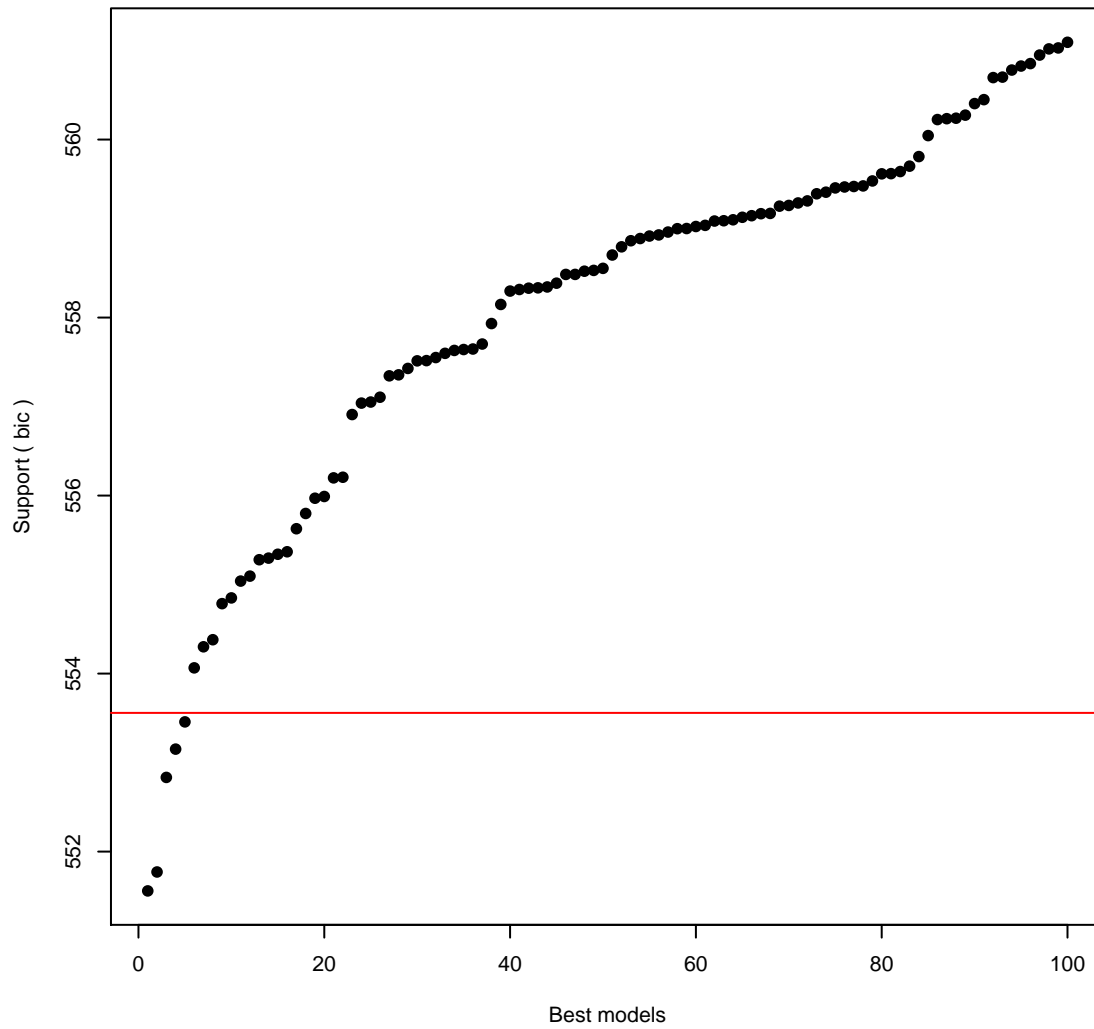
```
summary(asreg.result@objects[[1]])
```

```
## Call:
## fitfunc(formula = as.formula(x), data = data)
##
##   n= 110, number of events= 70
##
##           coef exp(coef) se(coef)      z Pr(>|z|)
## mg.5      2.81     16.65    1.08 2.60  0.0093
## mg.6      6.99    1089.19    1.19 5.87  4.4e-09
##
##      exp(coef) exp(-coef) lower .95 upper .95
## mg.5      16.7   0.060050      2     139
## mg.6    1089.2   0.000918    105    11264
##
## Concordance= 0.702 (se = 0.038 )
## Rsquare= 0.265 (max possible= 0.995 )
## Likelihood ratio test= 33.9 on 2 df,  p=4.29e-08
## Wald test               = 38.8 on 2 df,  p=3.77e-09
## Score (logrank) test = 42.9 on 2 df,  p=4.87e-10
```

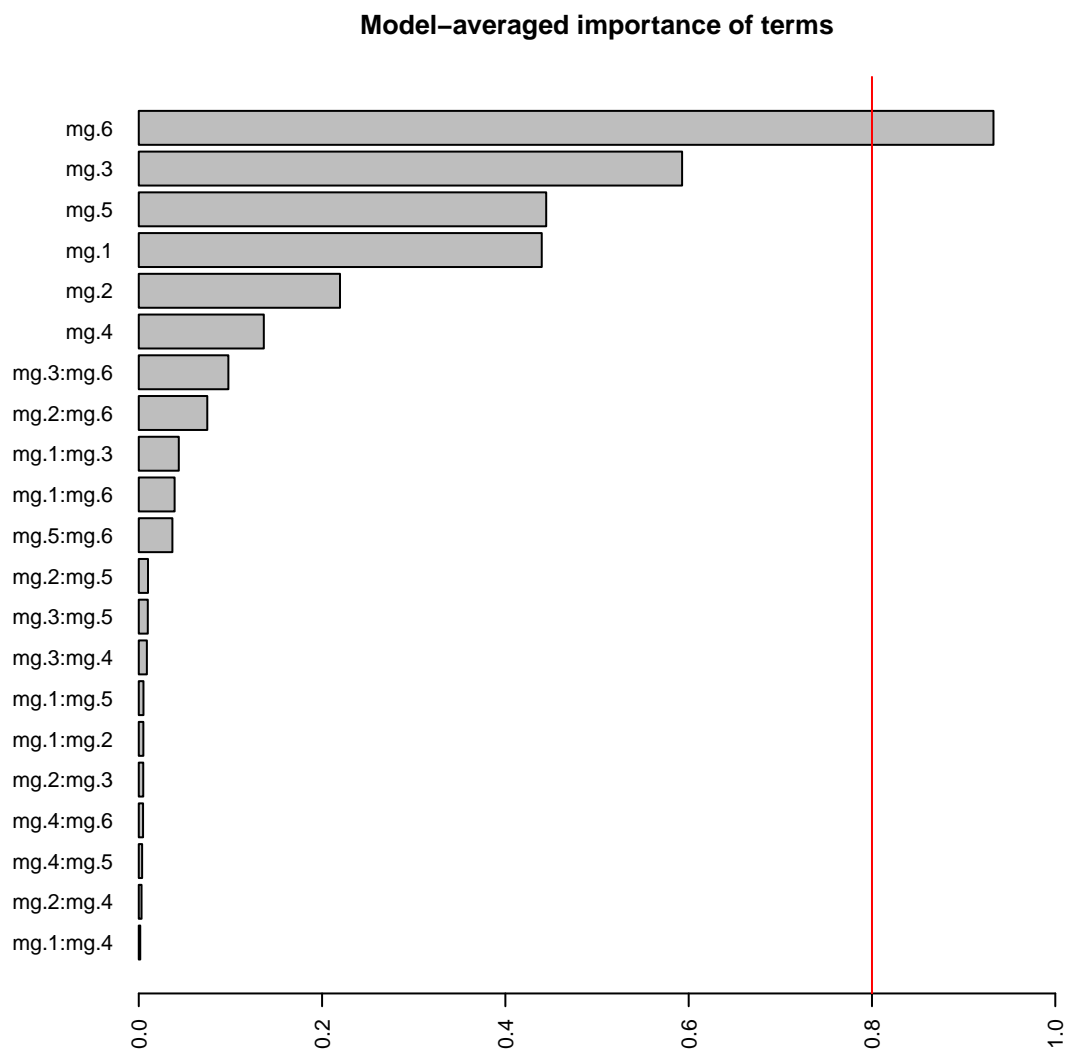
```
plot(asreg.result, type = "p")
```

All-subsets regression

IC profile

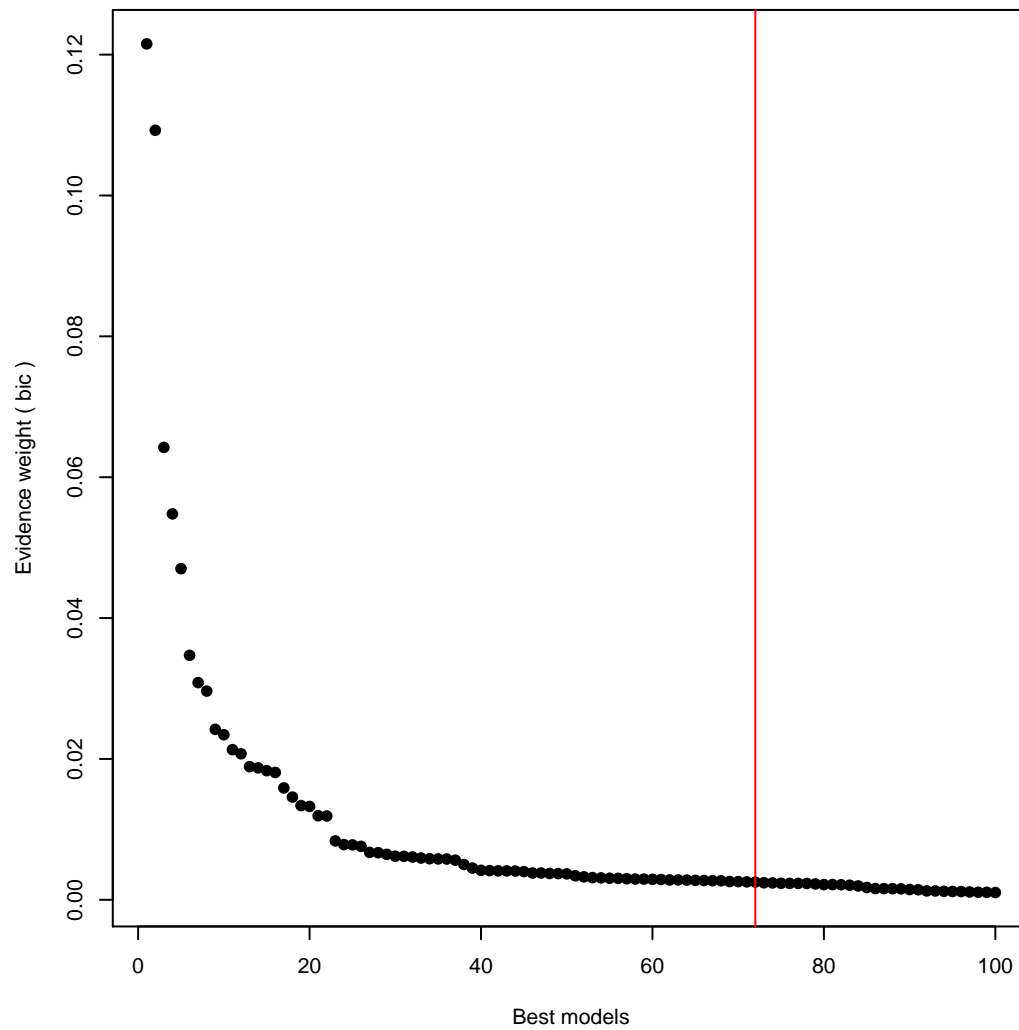


```
plot(asreg.result, type = "s")
```



```
plot(asreg.result, type = "w")
```


Profile of model weights



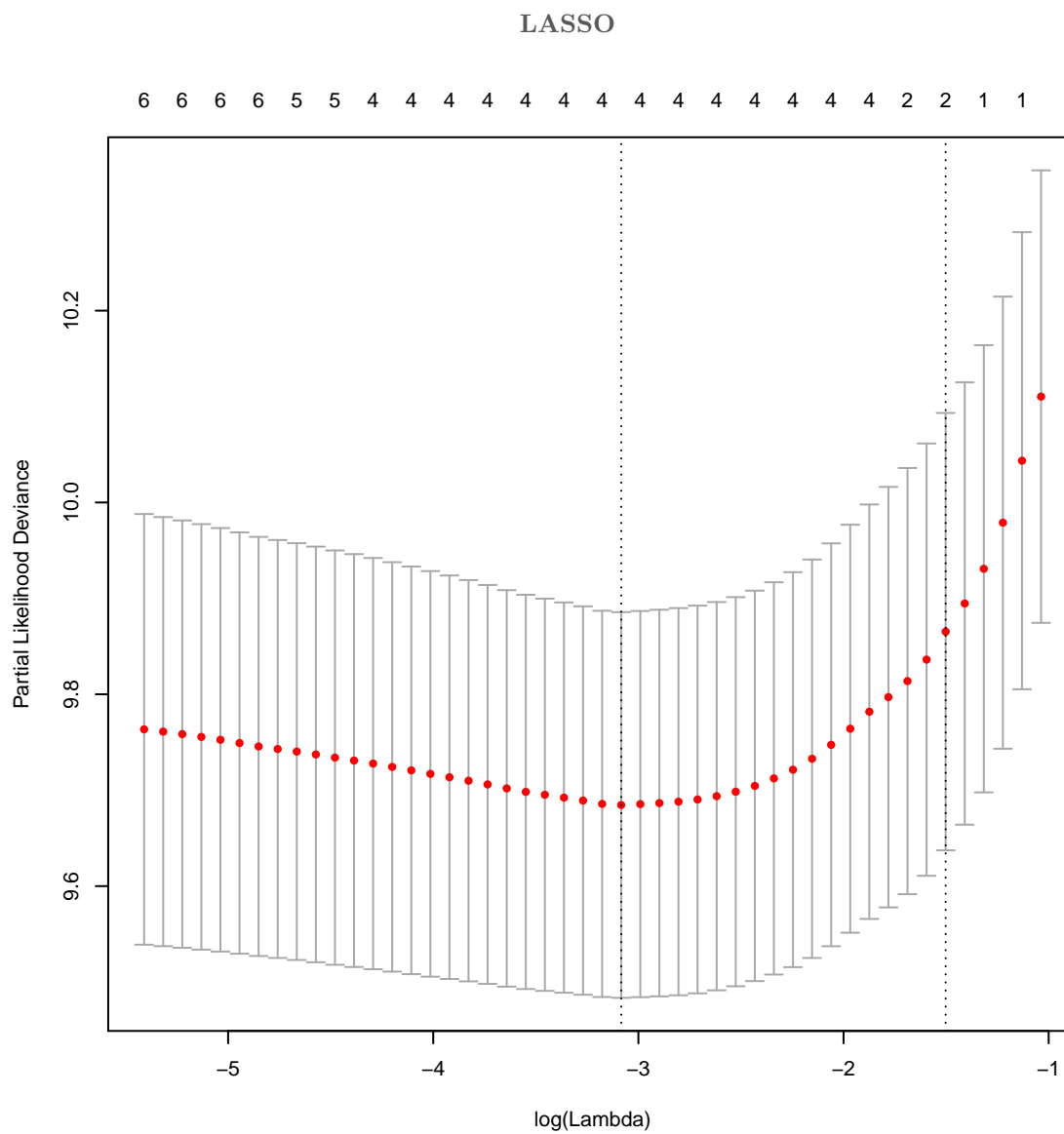
```
glmnet.coef.1se

## 6 x 1 sparse Matrix of class "dgCMatrix"
##           1
## mg.1  .
## mg.2  .
## mg.3 -0.1635
## mg.4  .
## mg.5  .
## mg.6  3.0808

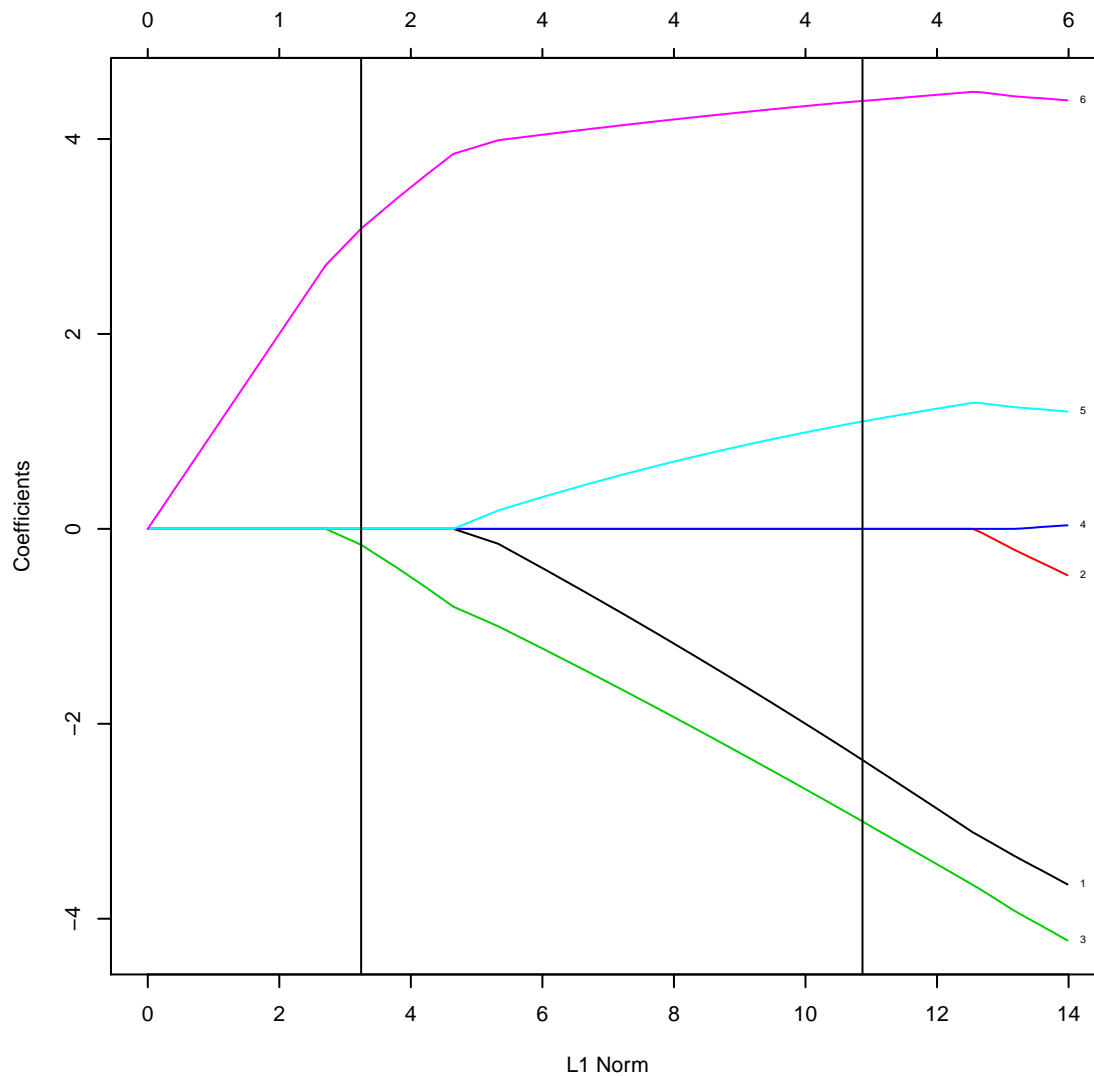
glmnet.coef.min
```

```
## 6 x 1 sparse Matrix of class "dgCMatrix"
##          1
## mg.1 -2.372
## mg.2  .
## mg.3 -3.002
## mg.4  .
## mg.5  1.102
## mg.6  4.391
```

```
plot(glmnet.fit.cv)
```



```
plot(glmnet.fit.cv$glmnet.fit, label = TRUE)
abline(v = sum(abs(glmnet.coef.1se)))
abline(v = sum(abs(glmnet.coef.min)))
```



4.3 Prediction on validation sets

```
load("../data/15_validation.rda")
```

```
val.basis = basis(nmf.final)
rownames(GSE21501.lingex) = GSE21501.feats$Gene.symbol
rownames(GSE28735.lingex) = GSE28735.feats$Gene.symbol
GSE21501.lingex.for_basis = GSE21501.lingex[match(rownames(val.basis), rownames(GSE21501.lingex)),
]
GSE28735.lingex.for_basis = GSE28735.lingex[match(rownames(val.basis), rownames(GSE28735.lingex)),
]
GSE21501.lingex.for_basis[is.na(GSE21501.lingex.for_basis)] = 0
GSE28735.lingex.for_basis[is.na(GSE28735.lingex.for_basis)] = 0
GSE21501.coefs = apply(GSE21501.lingex.for_basis, 2, function(xcol) nnls(val.basis,
```

```

xcol)$x)
GSE28735.coefs = apply(GSE28735.lingex.for_basis, 2, function(xcol) nnls(val.basis,
xcol)$x)

```

```

apply(GSE21501.coefs, 1, function(xc) coxph(Surv(time, event) ~ xc, data = GSE21501.samp))

## [[1]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z    p
## xc -5.31   0.00495    3.44 -1.54 0.12
##
## Likelihood ratio test=2.57 on 1 df, p=0.109 n= 102, number of events= 66
##
## [[2]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z    p
## xc  2.17      8.79      2.6 0.836 0.4
##
## Likelihood ratio test=0.68 on 1 df, p=0.41 n= 102, number of events= 66
##
## [[3]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z    p
## xc -1.09      0.337      2.73 -0.399 0.69
##
## Likelihood ratio test=0.16 on 1 df, p=0.688 n= 102, number of events= 66
##
## [[4]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z    p
## xc -0.226      0.798      2.47 -0.0914 0.93
##
## Likelihood ratio test=0.01 on 1 df, p=0.927 n= 102, number of events= 66
##
## [[5]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z    p
## xc  2.17      8.75      3.04 0.713 0.48

```

```
##
## Likelihood ratio test=0.49 on 1 df, p=0.486 n= 102, number of events= 66
##
## [[6]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## xc 2.57      13.1      2.08 1.24 0.22
##
## Likelihood ratio test=1.45 on 1 df, p=0.229 n= 102, number of events= 66

apply(GSE21501.coefs, 1, function(xc) coxph(Surv(time, event) ~ tstage + nstage +
      xc, data = GSE21501.samp))

## [[1]]
## Call:
## coxph(formula = Surv(time, event) ~ tstage + nstage + xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## tstage -0.166    0.84664    0.281 -0.593 0.550
## nstage  0.653    1.92135    0.315  2.074 0.038
## xc      -5.237    0.00532    3.545 -1.477 0.140
##
## Likelihood ratio test=7.13 on 3 df, p=0.0678 n= 97, number of events= 63
## (5 observations deleted due to missingness)
##
## [[2]]
## Call:
## coxph(formula = Surv(time, event) ~ tstage + nstage + xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## tstage -0.161    0.851    0.287 -0.560 0.580
## nstage  0.643    1.903    0.316  2.039 0.041
## xc      1.025    2.788    2.658  0.386 0.700
##
## Likelihood ratio test=4.94 on 3 df, p=0.176 n= 97, number of events= 63
## (5 observations deleted due to missingness)
##
## [[3]]
## Call:
## coxph(formula = Surv(time, event) ~ tstage + nstage + xc, data = GSE21501.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## tstage -0.153    0.858    0.286 -0.535 0.590
## nstage  0.659    1.933    0.314  2.097 0.036
## xc      -1.379    0.252    2.796 -0.493 0.620
##
## Likelihood ratio test=5.04 on 3 df, p=0.169 n= 97, number of events= 63
## (5 observations deleted due to missingness)
```

```
##
## [[4]]
## Call:
## coxph(formula = Surv(time, event) ~ tstage + nstage + xc, data = GSE21501.samp)
##
##
##          coef exp(coef) se(coef)      z      p
## tstage -0.158    0.854    0.285 -0.554 0.580
## nstage  0.678    1.970    0.319  2.126 0.034
## xc     -1.041    0.353    2.463 -0.423 0.670
##
## Likelihood ratio test=4.98 on 3 df, p=0.173 n= 97, number of events= 63
## (5 observations deleted due to missingness)
##
## [[5]]
## Call:
## coxph(formula = Surv(time, event) ~ tstage + nstage + xc, data = GSE21501.samp)
##
##
##          coef exp(coef) se(coef)      z      p
## tstage -0.179    0.836    0.289 -0.621 0.530
## nstage  0.641    1.898    0.315  2.033 0.042
## xc     1.878    6.543    3.313  0.567 0.570
##
## Likelihood ratio test=5.11 on 3 df, p=0.164 n= 97, number of events= 63
## (5 observations deleted due to missingness)
##
## [[6]]
## Call:
## coxph(formula = Surv(time, event) ~ tstage + nstage + xc, data = GSE21501.samp)
##
##
##          coef exp(coef) se(coef)      z      p
## tstage -0.110    0.896    0.284 -0.388 0.700
## nstage  0.657    1.928    0.316  2.077 0.038
## xc     2.510   12.310    2.164  1.160 0.250
##
## Likelihood ratio test=6.07 on 3 df, p=0.108 n= 97, number of events= 63
## (5 observations deleted due to missingness)

apply(GSE21501.coefs, 1, function(xc) anova(coxph(Surv(time, event) ~ tstage +
  nstage + xc, data = GSE21501.samp)))

## [[1]]
## Analysis of Deviance Table
## Cox model: response is Surv(time, event)
## Terms added sequentially (first to last)
##
##          loglik Chisq Df Pr(>|Chi|)
## NULL          -242
## tstage       -242  0.01  1      0.928
## nstage       -239  4.79  1      0.029
## xc           -238  2.34  1      0.126
##
```

```
## [[2]]
## Analysis of Deviance Table
## Cox model: response is Surv(time, event)
## Terms added sequentially (first to last)
##
##      loglik Chisq Df Pr(>|Chi|)
## NULL      -242
## tstage    -242  0.01  1      0.928
## nstage    -239  4.79  1      0.029
## xc        -239  0.15  1      0.702
##
## [[3]]
## Analysis of Deviance Table
## Cox model: response is Surv(time, event)
## Terms added sequentially (first to last)
##
##      loglik Chisq Df Pr(>|Chi|)
## NULL      -242
## tstage    -242  0.01  1      0.928
## nstage    -239  4.79  1      0.029
## xc        -239  0.25  1      0.619
##
## [[4]]
## Analysis of Deviance Table
## Cox model: response is Surv(time, event)
## Terms added sequentially (first to last)
##
##      loglik Chisq Df Pr(>|Chi|)
## NULL      -242
## tstage    -242  0.01  1      0.928
## nstage    -239  4.79  1      0.029
## xc        -239  0.18  1      0.668
##
## [[5]]
## Analysis of Deviance Table
## Cox model: response is Surv(time, event)
## Terms added sequentially (first to last)
##
##      loglik Chisq Df Pr(>|Chi|)
## NULL      -242
## tstage    -242  0.01  1      0.928
## nstage    -239  4.79  1      0.029
## xc        -239  0.31  1      0.577
##
## [[6]]
## Analysis of Deviance Table
## Cox model: response is Surv(time, event)
## Terms added sequentially (first to last)
##
##      loglik Chisq Df Pr(>|Chi|)
## NULL      -242
## tstage    -242  0.01  1      0.928
## nstage    -239  4.79  1      0.029
```

```
## xc      -239  1.27  1      0.259

apply(GSE28735.coefs, 1, function(xc) coxph(Surv(time, event) ~ xc, data = GSE28735.samp))

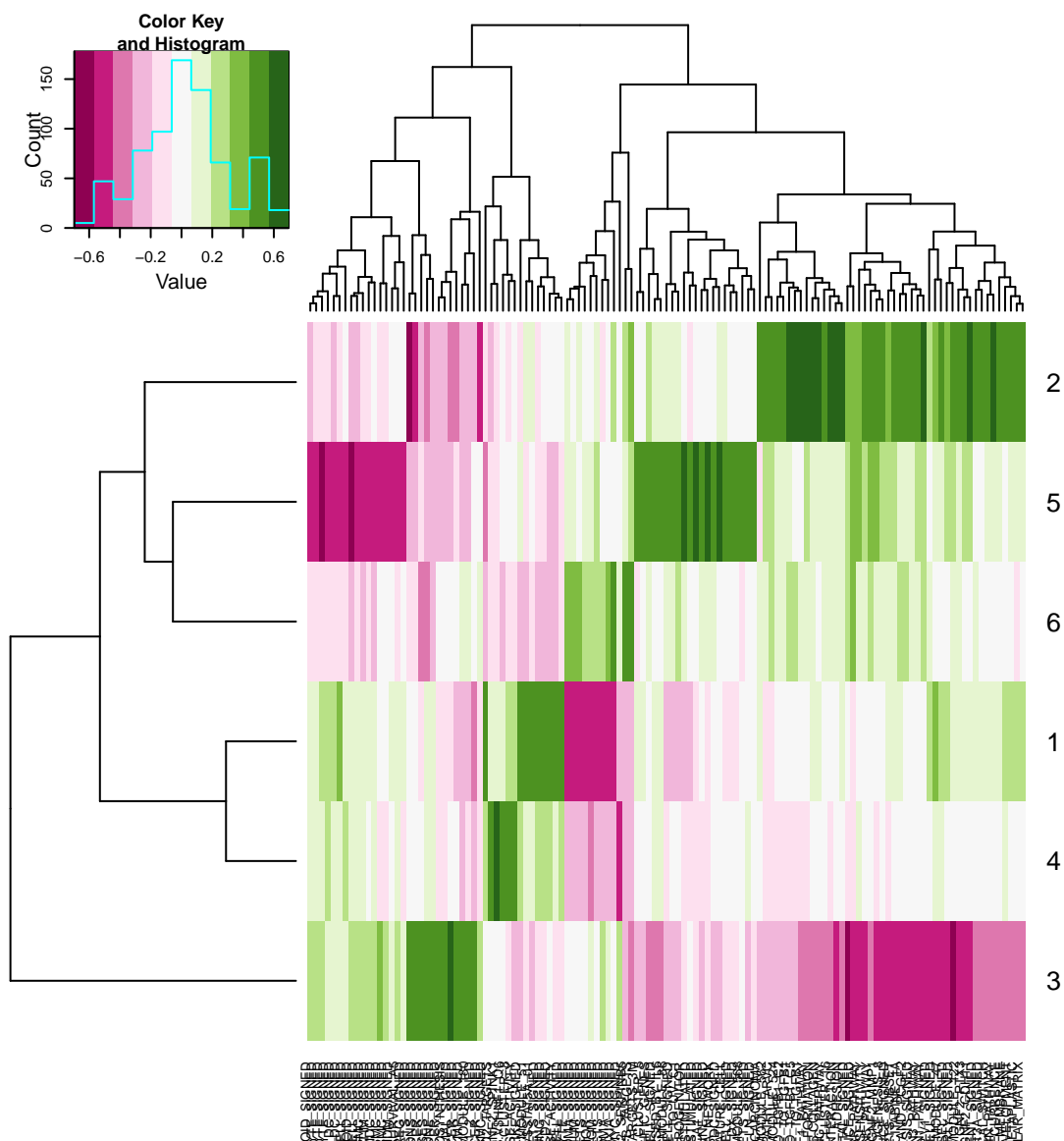
## [[1]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE28735.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## xc -4.5    0.0111    3.74 -1.2 0.23
##
## Likelihood ratio test=1.55 on 1 df, p=0.213 n= 42, number of events= 29
##
## [[2]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE28735.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## xc 3.46    31.7    2.53 1.36 0.17
##
## Likelihood ratio test=1.63 on 1 df, p=0.201 n= 42, number of events= 29
##
## [[3]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE28735.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## xc -7.79  0.000415    3.22 -2.42 0.015
##
## Likelihood ratio test=6.32 on 1 df, p=0.0119 n= 42, number of events= 29
##
## [[4]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE28735.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## xc 0.72    2.05    2.81 0.256 0.8
##
## Likelihood ratio test=0.06 on 1 df, p=0.801 n= 42, number of events= 29
##
## [[5]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE28735.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## xc -0.469    0.625    2.61 -0.18 0.86
##
## Likelihood ratio test=0.03 on 1 df, p=0.857 n= 42, number of events= 29
##
```



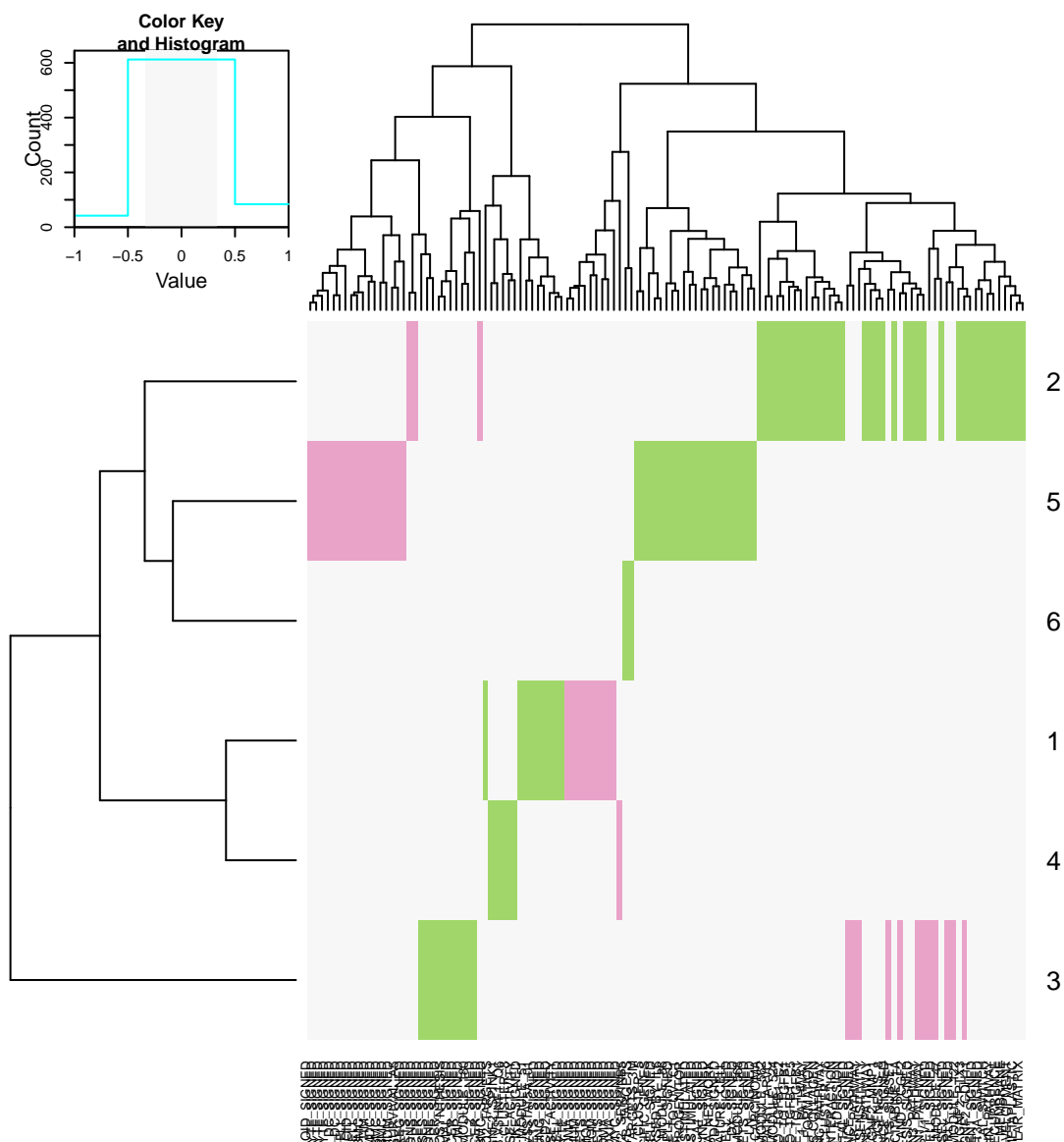
```
## [[6]]
## Call:
## coxph(formula = Surv(time, event) ~ xc, data = GSE28735.samp)
##
##
##      coef exp(coef) se(coef)      z      p
## xc 5.73      308      2.32 2.47 0.014
##
## Likelihood ratio test=5.68 on 1 df, p=0.0171 n= 42, number of events= 29
```

4.4 MSigDB score correlation thresholding

```
temp.sel_cols = apply(abs(nmf.final.msigdb.corr) >= sig.corr.threshold, 2, any)
heatmap.2(nmf.final.msigdb.corr[, temp.sel_cols], trace = "none", scale = "none",
          useRaster = TRUE, col = brewer.pal(11, "PiYG"), symbreaks = TRUE)
```



```
heatmap.2(nmf.final.msigdb.corr[, temp.sel_cols], trace = "none", scale = "none",
  useRaster = TRUE, col = brewer.pal(3, "PiYG"), breaks = c(-1, -sig.corr.threshold,
  sig.corr.threshold, 1))
```



```
temp.sig_id = colnames(nmf.final.msigdb.corr)
temp.sig_class = gsub("\\.*", "", temp.sig_id)
temp.nsig = length(temp.sig_id)
temp.nmeta = nrow(nmf.final.msigdb.corr)
tables = lapply(1:temp.nmeta, function(metagene_i) {
  tapply(1:temp.nsig, temp.sig_class, function(sig_class_is) {
    all_cors = nmf.final.msigdb.corr[, sig_class_is]
    this_cors = all_cors[metagene_i, ]
    this_ids = temp.sig_id[sig_class_is]

    all_sig_cors = abs(all_cors) >= sig.corr.threshold
    this_sig_cors = all_sig_cors[metagene_i, ]
```

```

sigs_to_report = which(this_sig_cors)

if (length(sigs_to_report) == 0) {
  table = data.frame(GeneSet = c(), Correlation = c(), Metagenes = c())
} else {
  table = data.frame(GeneSet = this_ids[sigs_to_report], Correlation = this_cors[sigs_to_report],
    Metagenes = apply(all_cors[, sigs_to_report, drop = FALSE],
      2, function(cors) {
        sel = abs(cors) >= sig.corr.threshold
        # A positive number implies that positive GSVA signal is associated with
        # worse prognosis
        paste(which(sel) * sign(cors[which(sel)]) * sign(nmf.final.cpv.pvals$surv.diag_dsd.
          collapse = ","))
      })
  table = table[order(-(table$Correlation)), ]
  rownames(table) <- NULL
}
table
}, simplify = FALSE)
})
tables

## [[1]]
## [[1]]$c1
## data frame with 0 columns and 0 rows
##
## [[1]]$c2
##
##           GeneSet Correlation Metagenes
## 1      c2.KATSANOUELAVL1_TARGETS_SIGNED      0.5096      -1
## 2      c2.ZHAN_MULTIPLE_MYELOMA_CD2_SIGNED      0.5086      -1
## 3      c2.SMID_BREAST_CANCER_NORMAL_LIKE_SIGNED      0.5080      -1
## 4      c2.GREENBAUM_E2A_TARGETS_SIGNED     -0.5009       1
## 5 c2.MARTORIATI_MDM4_TARGETS_NEUROEPITHELIUM_SIGNED     -0.5012       1
## 6      c2.YU_MYC_TARGETS_SIGNED     -0.5029       1
## 7      c2.SABATES_COLORECTAL_ADENOMA_SIGNED     -0.5036       1
## 8      c2.WINTER_HYPOXIA_SIGNED     -0.5241       1
## 9      c2.WEST_ADRENOCORTICAL_TUMOR_SIGNED     -0.5416       1
## 10     c2.SHIPP_DLBCL_VS_FOLLICULAR_LYMPHOMA_SIGNED     -0.5500       1
## 11     c2.LEE_EARLY_T_LYMPHOCYTE_SIGNED     -0.5517       1
## 12     c2.HAHTOLA_SEZARY_SYNDROM_SIGNED     -0.5641       1
##
## [[1]]$c3
##           GeneSet Correlation Metagenes
## 1 c3.V$STAT5A_01      0.5234      -1
##
## [[1]]$c4
##           GeneSet Correlation Metagenes
## 1 c4.MODULE_51      0.5399      -1
##
## [[1]]$c5
##           GeneSet Correlation Metagenes
## 1 c5.PHOSPHORIC_DIESTER_HYDROLASE_ACTIVITY      0.5113      -1
##
## [[1]]$c6

```

```

## data frame with 0 columns and 0 rows
##
## [[1]]$c7
##                                     GeneSet Correlation
## 1          c7.GSE20715_OH_VS_48H_OZONE_TLR4_KO_LUNG_SIGNED      0.5160
## 2 c7.GSE22886_IGM_MEMORY_BCELL_VS_BLOOD_PLASMA_CELL_SIGNED      0.5019
## 3          c7.GSE34205_HEALTHY_VS_RSV_INF_INFANT_PBMK_SIGNED      0.5002
##   Metagenes
## 1         -1
## 2         -1
## 3         -1
##
##
## [[2]]
## [[2]]$c1
## data frame with 0 columns and 0 rows
##
## [[2]]$c2
##
##                                     Gen
## 1          c2.REACTOME_EXTRACELLULAR_MATRIX_ORGANIZATION/c2.REACTOME_COLLAGEN_FORMA
## 2                                     c2.PID_SYNDECAN_1_PAT
## 3          c2.VERRECCHIA_DELAYED_RESPONSE_TO_T
## 4                                     c2.PID_INTEGRIN1_PAT
## 5                                     c2.PID_AVB3_INTEGRIN_PAT
## 6 c2.FARMER_BREAST_CANCER_CLUSTER_5/c2.ANASTASSIOU_CANCER_MESENCHYMAL_TRANSITION_SIGNATURE/c4.GNF2_C
## 7          c2.YAO_TEMPORAL_RESPONSE_TO_PROGESTERONE_CLUSTER
## 8                                     c2.KEGG_ECM_RECEPTOR_INTERAC
## 9          c2.VERRECCHIA_RESPONSE_TO_TGFB
## 10          c2.VERRECCHIA_EARLY_RESPONSE_TO_T
## 11          c2.KEGG_FOCAL_ADHE
## 12          c2.MAHADEVAN_GIST_MORPHOLOGICAL_SW
## 13          c2.CAIRO_LIVER_DEVELOPMENT_SI
## 14          c2.PID_INTEGRIN3_PAT
## 15          c2.KEGG_BASAL_CELL_CARCI
## 16          c2.BURTON_ADIPOGENES
## 17          c2.VERRECCHIA_RESPONSE_TO_TGFB
## 18          c2.CROMER_TUMORIGENESIS_SI
## 19          c2.WIEDERSCHAIN_TARGETS_OF_BMI1_AND_F
## 20          c2.ROZANOV_MMP14_TARGETS_SU
## 21          c2.PID_WNT_SIGNALING_PAT
## 22          c2.KEGG_ARRHYTHMOGENIC_RIGHT_VENTRICULAR_CARDIOMYOPATHY
## 23          c2.LABBE_TARGETS_OF_TGFB1_AND_WNT3A_SI
## 24          c2.LIEN_BREAST_CARCINOMA_METAPLA
## 25          c2.PID_INTEGRIN5_PAT
## 26          c2.LINDGREN_BLADDER_CANCER_HIGH_RECURREN
## 27          c2.POTTI_TOPOTECAN_SENSITI
## 28          c2.MIYAGAWA_TARGETS_OF_EWSR1_ETS_FUSIONS_SI
## 29          c2.BERTUCCI_MEDULLARY_VS_DUCTAL_BREAST_CANCER_SI
## 30          c2.PASINI_SUZ12_TARGETS_SI
##   Correlation Metagenes
## 1         0.6490      2
## 2         0.6355      2
## 3         0.6178      2
## 4         0.6067    2,-3

```

```

## 5      0.6020      2
## 6      0.5990      2
## 7      0.5963      2
## 8      0.5953      2
## 9      0.5849      2
## 10     0.5829      2
## 11     0.5758      2
## 12     0.5587      2
## 13     0.5429      2
## 14     0.5409      2,-3
## 15     0.5396      2
## 16     0.5346      2
## 17     0.5312      2
## 18     0.5258      2
## 19     0.5242      2
## 20     0.5228      2
## 21     0.5171      2
## 22     0.5114      2
## 23     0.5081      2
## 24     0.5077      2
## 25     0.5074      2
## 26     0.5047      2
## 27     0.5017      2
## 28     -0.5087     -2
## 29     -0.5436     -2
## 30     -0.5916     -2
##
## [[2]]$c3
## data frame with 0 columns and 0 rows
##
## [[2]]$c4
##
##           GeneSet Correlation Metagenes
## 1      c4.GNF2_PTX3      0.5533      2,-3
## 2      c4.MODULE_122      0.5369      2
## 3      c4.GNF2_MMP1      0.5366      2
## 4      c4.MODULE_562      0.5178      2
## 5 c4.MODULE_419/c4.MODULE_524      0.5128      2
## 6      c4.MODULE_47      0.5003      2
##
## [[2]]$c5
##
##                                     GeneSet
## 1                                     c5.COLLAGEN
## 2 c5.PROTEINACEOUS_EXTRACELLULAR_MATRIX/c5.EXTRACELLULAR_MATRIX_PART/c5.EXTRACELLULAR_MATRIX
## 3                                     c5.BASEMENT_MEMBRANE
## 4                                     c5.SKELETAL_DEVELOPMENT
## Correlation Metagenes
## 1      0.6496      2
## 2      0.5336      2
## 3      0.5148      2
## 4      0.5101      2
##
## [[2]]$c6
## data frame with 0 columns and 0 rows
##

```

```
## [[2]]$c7
## data frame with 0 columns and 0 rows
##
##
## [[3]]
## [[3]]$c1
## data frame with 0 columns and 0 rows
##
## [[3]]$c2
##
##                                     GeneSet Correlation
## 1  c2.CHARAFE_BREAST_CANCER_LUMINAL_VS_MESENCHYMAL_SIGNED      0.5882
## 2                c2.REACTOME_GLYCEROPHOSPHOLIPID_BIOSYNTHESIS    0.5269
## 3                c2.SMID_BREAST_CANCER_RELAPSE_IN_BONE_SIGNED    0.5215
## 4                        c2.LIU_PROSTATE_CANCER_SIGNED           0.5202
## 5                c2.WAMUNYOKOLI_OVARIAN_CANCER_GRADES_1_2_SIGNED  0.5178
## 6  c2.WANG_BARRETTS_ESOPHAGUS_AND_ESOPHAGUS_CANCER_SIGNED      0.5175
## 7                c2.WAMUNYOKOLI_OVARIAN_CANCER_LMP_SIGNED       0.5165
## 8                        c2.WALLACE_PROSTATE_CANCER_SIGNED       0.5155
## 9                c2.DOANE_BREAST_CANCER_CLASSES_SIGNED          0.5111
## 10                   c2.WOO_LIVER_CANCER_RECURRENCE_SIGNED      -0.5000
## 11                        c2.PID_UPA_UPAR_PATHWAY               -0.5011
## 12                c2.SUZUKI_RESPONSE_TO_TSA_AND_DECITABINE_1A   -0.5141
## 13                   c2.HUANG_DASATINIB_RESISTANCE_SIGNED       -0.5145
## 14                        c2.LIM_MAMMARY_STEM_CELL_SIGNED       -0.5175
## 15                        c2.PID_INTEGRIN3_PATHWAY               -0.5175
## 16                   c2.ROY_WOUND_BLOOD_VESSEL_SIGNED          -0.5235
## 17                        c2.PID_INTEGRIN1_PATHWAY               -0.5248
## 18  c2.LIEN_BREAST_CARCINOMA_METAPLASTIC_VS_DUCTAL_SIGNED      -0.6110
## 19                c2.VECCHI_GASTRIC_CANCER_ADVANCED_VS_EARLY_SIGNED -0.6217
## Metagenes
## 1                -3
## 2                -3
## 3                -3
## 4                -3
## 5                -3
## 6                -3
## 7                -3
## 8                -3
## 9                -3
## 10               3
## 11               3
## 12               3
## 13               3
## 14               3
## 15             -2,3
## 16               3
## 17             -2,3
## 18               3
## 19               3
##
## [[3]]$c3
## data frame with 0 columns and 0 rows
##
```

```

## [[3]]$c4
##                               GeneSet Correlation Metagenes
## 1 c4.MODULE_139/c4.MODULE_180      0.5195      -3
## 2                c4.GNF2_PTX3     -0.5155      -2,3
##
## [[3]]$c5
## data frame with 0 columns and 0 rows
##
## [[3]]$c6
##                               GeneSet Correlation Metagenes
## 1 c6.LEF1_UP.V1_SIGNED      -0.5597      3
##
## [[3]]$c7
## data frame with 0 columns and 0 rows
##
##
## [[4]]
## [[4]]$c1
## data frame with 0 columns and 0 rows
##
## [[4]]$c2
##                               GeneSet Correlation Metagenes
## 1                c2.BERGER_MBD2_TARGETS      0.5646      -4
## 2 c2.TERAMOTO_OPN_TARGETS_CLUSTER_8      0.5274      -4
## 3      c2.LEE_LIVER_CANCER_MYC_SIGNED     -0.5203      4
##
## [[4]]$c3
##                               GeneSet Correlation Metagenes
## 1 c3.V$HNF1_Q6      0.5124      -4
##
## [[4]]$c4
##                               GeneSet Correlation Metagenes
## 1 c4.GNF2_SERPINI2/c4.GNF2_SPINK1      0.6959      -4
##
## [[4]]$c5
##                               GeneSet Correlation Metagenes
## 1 c5.CARBOXYPEPTIDASE_ACTIVITY      0.5342      -4
##
## [[4]]$c6
## data frame with 0 columns and 0 rows
##
## [[4]]$c7
## data frame with 0 columns and 0 rows
##
##
## [[5]]
## [[5]]$c1
## data frame with 0 columns and 0 rows
##
## [[5]]$c2
##                               GeneSet
## 1 c2.IVANOVA_HEMATOPOIESIS_LATE_PROGENITOR
## 2 c2.MARSON_BOUND_BY_FOXP3_STIMULATED

```

```

## 3 c2.SESTO_RESPONSE_TO_UV_C1
## 4 c2.NAKAYAMA_SOFT_TISSUE_TUMORS_PCA1_SIGNED
## 5 c2.IVANOVA_HEMATOPOIESIS_MATURE_CELL
## 6 c2.MARTINEZ_RB1_AND_TP53_TARGETS_SIGNED/c2.MARTINEZ_TP53_TARGETS_SIGNED
## 7 c2.KAMIKUBO_MYELOID_CEBPA_NETWORK
## 8 c2.MARSON_BOUND_BY_FOXP3_UNSTIMULATED
## 9 c2.VALK_AML_CLUSTER_5
## 10 c2.RAGHAVACHARI_PLATELET_SPECIFIC_GENES
## 11 c2.LIAN_LIPA_TARGETS_6M/c2.LIAN_LIPA_TARGETS_3M
## 12 c2.BROCKE_APOPTOSIS_REVERSED_BY_IL6
## 13 c2.SHEDDEN_LUNG_CANCER_GOOD_SURVIVAL_A5
## Correlation Metagenes
## 1 0.6114 5
## 2 0.5798 5
## 3 0.5491 5
## 4 0.5413 5
## 5 0.5410 5
## 6 0.5304 5
## 7 0.5280 5
## 8 0.5154 5
## 9 0.5134 5
## 10 0.5124 5
## 11 0.5005 5
## 12 0.5001 5
## 13 -0.5080 -5
##
## [[5]]$c3
## data frame with 0 columns and 0 rows
##
## [[5]]$c4
## GeneSet Correlation Metagenes
## 1 c4.MODULE_86 0.5240 5
## 2 c4.MODULE_491/c4.MODULE_568 0.5063 5
##
## [[5]]$c5
## data frame with 0 columns and 0 rows
##
## [[5]]$c6
## data frame with 0 columns and 0 rows
##
## [[5]]$c7
## GeneSet
## 1 c7.GSE29618_MONOCYTE_VS_PDC_SIGNED
## 2 c7.GSE29618_MONOCYTE_VS_PDC_DAY7_FLU_VACCINE_SIGNED
## 3 c7.GSE3982_MAC_VS_NKCELL_SIGNED
## 4 c7.GSE15767_MED_VS_SCS_MAC_LN_SIGNED
## 5 c7.GSE3982_BASOPHIL_VS_CENT_MEMORY_CD4_TCELL_SIGNED
## 6 c7.GSE11057_PBMC_VS_MEM_CD4_TCELL_SIGNED
## 7 c7.GSE9006_HEALTHY_VS_TYPE_1_DIABETES_PBMC_4MONTH_POST_DX_SIGNED
## 8 c7.GSE11057_NAIVE_CD4_VS_PBMC_CD4_TCELL_SIGNED
## 9 c7.GSE3982_DC_VS_MAC_LPS_STIM_SIGNED
## 10 c7.GSE17721_POLYIC_VS_GARDIQUIMOD_1H_BMDM_SIGNED
## 11 c7.GSE29618_PDC_VS_MDC_SIGNED
## 12 c7.GSE6269_HEALTHY_VS_STREP_AUREUS_INF_PBMC_SIGNED

```



```

## 13          c7.GSE20366_CD103_KLRG1_DP_VS_DN_TREG_SIGNED
## 14          c7.GSE22886_NAIVE_CD8_TCELL_VS_DC_SIGNED
## 15          c7.GSE22886_NAIVE_CD8_TCELL_VS_MONOCYTE_SIGNED
## 16          c7.GSE11057_CD4_CENT_MEM_VS_PBMC_SIGNED
## 17          c7.GSE22886_NAIVE_CD4_TCELL_VS_DC_SIGNED
## 18          c7.GSE11057_NAIVE_VS_MEMORY_CD4_TCELL_SIGNED
## 19          c7.GSE11057_CD4_EFF_MEM_VS_PBMC_SIGNED
## 20          c7.GSE10325_BCELL_VS_MYELOID_SIGNED
## 21          c7.GSE22886_NAIVE_TCELL_VS_MONOCYTE_SIGNED
## 22          c7.GSE10325_LUPUS_CD4_TCELL_VS_LUPUS_MYELOID_SIGNED
## 23          c7.GSE22886_NAIVE_CD4_TCELL_VS_MONOCYTE_SIGNED
##      Correlation Metagenes
## 1      0.5760      5
## 2      0.5712      5
## 3      0.5573      5
## 4      0.5502      5
## 5      0.5352      5
## 6      0.5314      5
## 7      0.5209      5
## 8     -0.5042     -5
## 9     -0.5042     -5
## 10     -0.5076     -5
## 11     -0.5086     -5
## 12     -0.5086     -5
## 13     -0.5233     -5
## 14     -0.5267     -5
## 15     -0.5274     -5
## 16     -0.5352     -5
## 17     -0.5355     -5
## 18     -0.5379     -5
## 19     -0.5420     -5
## 20     -0.5519     -5
## 21     -0.5610     -5
## 22     -0.5699     -5
## 23     -0.5825     -5
##
##
## [[6]]
## [[6]]$c1
## data frame with 0 columns and 0 rows
##
## [[6]]$c2
##      GeneSet Correlation Metagenes
## 1 c2.LEI_MYB_TARGETS      0.509      6
##
## [[6]]$c3
## data frame with 0 columns and 0 rows
##
## [[6]]$c4
##      GeneSet Correlation Metagenes
## 1 c4.GNF2_CDH3/c4.GNF2_SERPINB5      0.5532      6
##
## [[6]]$c5
## data frame with 0 columns and 0 rows

```

```
##
## [[6]]$c6
## data frame with 0 columns and 0 rows
##
## [[6]]$c7
## data frame with 0 columns and 0 rows
```

5 Session information

```
session_info

## R version 3.1.1 (2014-07-10)
## Platform: x86_64-unknown-linux-gnu (64-bit)
##
## locale:
##  [1] LC_CTYPE=en_AU.UTF-8      LC_NUMERIC=C
##  [3] LC_TIME=en_AU.UTF-8      LC_COLLATE=en_AU.UTF-8
##  [5] LC_MONETARY=en_AU.UTF-8  LC_MESSAGES=en_AU.UTF-8
##  [7] LC_PAPER=en_AU.UTF-8     LC_NAME=en_AU.UTF-8
##  [9] LC_ADDRESS=en_AU.UTF-8   LC_TELEPHONE=en_AU.UTF-8
## [11] LC_MEASUREMENT=en_AU.UTF-8 LC_IDENTIFICATION=en_AU.UTF-8
##
## attached base packages:
## [1] splines    parallel  methods    stats      graphics  grDevices  utils
## [8] datasets  base
##
## other attached packages:
##  [1] doParallel_1.0.8    iterators_1.0.7    foreach_1.4.2
##  [4] ahaz_1.14           survival_2.37-7    NMF_0.20.5
##  [7] Biobase_2.26.0      BiocGenerics_0.12.1 cluster_1.15.3
## [10] rngtools_1.2.4      pkgmaker_0.22      registry_0.2
## [13] energy_1.6.2        glmnet_1.9-8       Matrix_1.1-4
## [16] glmulti_1.0.7       rJava_0.9-6
##
## loaded via a namespace (and not attached):
##  [1] boot_1.3-13         codetools_0.2-9    colorspace_1.2-4
##  [4] compiler_3.1.1      digest_0.6.4       ggplot2_1.0.0
##  [7] grid_3.1.1          gridBase_0.4-7     gtable_0.1.2
## [10] lattice_0.20-29     MASS_7.3-35        munsell_0.4.2
## [13] plyr_1.8.1          proto_0.3-10       RColorBrewer_1.0-5
## [16] Rcpp_0.11.3         reshape2_1.4       scales_0.2.4
## [19] stringr_0.6.2       tools_3.1.1        xtable_1.7-4

sessionInfo()

## R version 3.1.1 (2014-07-10)
## Platform: x86_64-unknown-linux-gnu (64-bit)
##
## locale:
##  [1] LC_CTYPE=en_AU.UTF-8      LC_NUMERIC=C
##  [3] LC_TIME=en_AU.UTF-8      LC_COLLATE=en_AU.UTF-8
##  [5] LC_MONETARY=en_AU.UTF-8  LC_MESSAGES=en_AU.UTF-8
```

```

## [7] LC_PAPER=en_AU.UTF-8          LC_NAME=en_AU.UTF-8
## [9] LC_ADDRESS=en_AU.UTF-8        LC_TELEPHONE=en_AU.UTF-8
## [11] LC_MEASUREMENT=en_AU.UTF-8    LC_IDENTIFICATION=en_AU.UTF-8
##
## attached base packages:
## [1] parallel  methods  splines  stats      graphics  grDevices  utils
## [8] datasets  base
##
## other attached packages:
## [1] stargazer_5.1          xtable_1.7-4          gplots_2.14.2
## [4] RColorBrewer_1.0-5    glmnet_1.9-8          Matrix_1.1-4
## [7] glmulti_1.0.7         rJava_0.9-6           nnls_1.4
## [10] NMF_0.20.5            Biobase_2.26.0        BiocGenerics_0.12.1
## [13] cluster_1.15.3        rngtools_1.2.4        pkgmaker_0.22
## [16] registry_0.2          energy_1.6.2          survival_2.37-7
## [19] knitr_1.8
##
## loaded via a namespace (and not attached):
## [1] bitops_1.0-6          boot_1.3-13           caTools_1.17.1
## [4] codetools_0.2-9       colorspace_1.2-4      digest_0.6.4
## [7] doParallel_1.0.8      evaluate_0.5.5        foreach_1.4.2
## [10] formatR_1.0           gdata_2.13.3          ggplot2_1.0.0
## [13] grid_3.1.1           gridBase_0.4-7        gtable_0.1.2
## [16] gtools_3.4.1         highr_0.4             iterators_1.0.7
## [19] KernSmooth_2.23-13    labeling_0.3          lattice_0.20-29
## [22] MASS_7.3-35          munsell_0.4.2         plyr_1.8.1
## [25] proto_0.3-10         Rcpp_0.11.3           reshape2_1.4
## [28] scales_0.2.4         stringr_0.6.2         tools_3.1.1

```