TOPMed CAMP DNA methylation betas cleaning

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Contents

1 Setup

```
# restart R session
#.rs.restartR()
rm(list=ls())

options(mc.cores=5)
system("hostname")
print(Sys.Date())

## [1] "2021-05-12"

print(Sys.time())

## [1] "2021-05-12 10:38:00 EDT"

# To generate document:
# Change working directory to code directory
# Run this code on toques using:
# module load R/4.0.3
#R -e 'library(knitr);knit("TOPMed_CAMP_betas_clean.Rnw")'
# pdflatex TOPMed_CAMP_betas_clean.tex

# merging with WGS, uses hg38?
## load libraries
libs <- c("IlluminaHumanMethylationEPICanno.ilm10b4.hg19",
          "IlluminaHumanMethylationEPICmanifest", "minfi")

for (l in libs) {
  if (require(l, character.only = T)) {
    print(paste0(l, " loaded successfully"))
  } else {
    install.packages(l)
    require(l, character.only = T)
    print(paste0(l, " installed and loaded successfully"))
  }
}

## [1] "IlluminaHumanMethylationEPICanno.ilm10b4.hg19 loaded successfully"
## [1] "IlluminaHumanMethylationEPICmanifest loaded successfully"
## [1] "minfi loaded successfully"

sig_digits <- 2
sum_sd <- function(data, varname) {
  eval(parse(text = str_c("data[, round(summary(", varname, "), digits=2)] %>% print()")))
  eval(parse(text = str_c("print(str_c('SD: ', data[, sd(", varname, ", na.rm = T) %>%
                                round(sig_digits)]))")))
}
```

1.1 Packages, Data locations and loading

```
qc.dir = "/proj/regeps/regep00/studies/CAMP"
camp.dir = file.path(qc.dir,"data/epigenetic/methylation/TopMed/data/freezes/20200117")

# loading rest of the libraries
libs <- c("limma", "wateRmelon", "minfi", "gplots", "ggplot2", "knitr", "R.utils", "impute",
      "stats", "tidyverse", "data.table", "here", "e1071", "GGally", "ggrepel", "ENmix",
      "meffil", "data.table", "robustbase", "stringi", "geneplotter", "RColorBrewer",
      "colorRamps", "lumi","ggrepel")
```

```
for (l in libs) {
  if (require(l, character.only = T)) {
    print(paste0(l, " loaded successfully"))
  } else {
    install.packages(l)
    require(l, character.only = T)
    print(paste0(l, " installed and loaded successfully"))
  }
}

## [1] "limma loaded successfully"
## [1] "wateRmelon loaded successfully"
## [1] "minfi loaded successfully"
## [1] "gplots loaded successfully"
## [1] "ggplot2 loaded successfully"
## [1] "knitr loaded successfully"
## [1] "R.utils loaded successfully"
## [1] "impute loaded successfully"
## [1] "stats loaded successfully"
## [1] "tidyverse loaded successfully"
## [1] "data.table loaded successfully"
## [1] "here loaded successfully"
## [1] "e1071 loaded successfully"
## [1] "GGally loaded successfully"
## [1] "ggrepel loaded successfully"
## [1] "ENmix loaded successfully"
## [1] "meffil loaded successfully"
## [1] "data.table loaded successfully"
## [1] "robustbase loaded successfully"
## [1] "stringi loaded successfully"
## [1] "geneplotter loaded successfully"
## [1] "RColorBrewer loaded successfully"
## [1] "colorRamps loaded successfully"
## [1] "lumi loaded successfully"
## [1] "ggrepel loaded successfully"

plots.dir = file.path(qc.dir,"analyses/reprk/methylation/plots")
results.dir = file.path(plots.dir,"../results")
meff.dir = file.path(qc.dir,"analyses/reprk/meffil_850K")

# scripts/code directory
setwd("/udd/reprk/projects/TOPMed/scripts")
# modified RCP code
source("RCP_mod.R")
source("LociWithSnps.R")

pca.betas <- function (beta, npc = 50)
{
    if (!is.matrix(beta)) {
        stop("beta is not a data matirx")
    }
    cat("Analysis is running, please wait...!", "\n")
    npc <- min(ncol(beta), npc)
    svd <- prcomp(t(beta), center = TRUE, scale = TRUE, retx = TRUE)
    eigenvalue <- svd[["sdev"]]^2
    prop <- (sum(eigenvalue[1:npc])/sum(eigenvalue)) * 100
    cat("Top ", npc, " principal components can explain ", prop,
        "% of data \n    variation", "\n")
    save(svd, eigenvalue, prop, file=file.path(results.dir,"pca_betas_auto_CAMP.RData"))
}

camp.pheno <- read.csv(file=file.path(qc.dir, "data/phenotype/camp_pheno_0421.csv"),
                 as.is=TRUE, sep=",", stringsAsFactors=FALSE)

samplesheet.camp <- read.csv(file=file.path(camp.dir, "LEVEL1/SampleSheet.csv"),
                             as.is=TRUE, sep = ",", fill=T, stringsAsFactors=FALSE)

# camp chanmine issues
#https://chanmine.bwh.harvard.edu/issues/21110

# Save result files with timeStamp
timeStamp <- as.character(round(unclass(Sys.time())))
print(timeStamp)

## [1] "1620830489"

# Resource: https://github.com/markgene/maxprobes
cross_probes_file = paste(camp.dir, "/LEVEL2/cross_reactive_probes.txt",
                          sep = "")
if (!file.size(cross_probes_file) == 0){
    cross_probes = read.table(cross_probes_file, sep = "\t",
                          header = F, quote = "\"", fill = T)
    colnames(cross_probes) = c("sample")
    n_cross_probes = nrow(cross_probes)
    n_cross_probes
} else {
    n_cross_probes = 0
}

## [1] 44570

n_cross_probes # 44,570

## [1] 44570
```

2 Mset loading

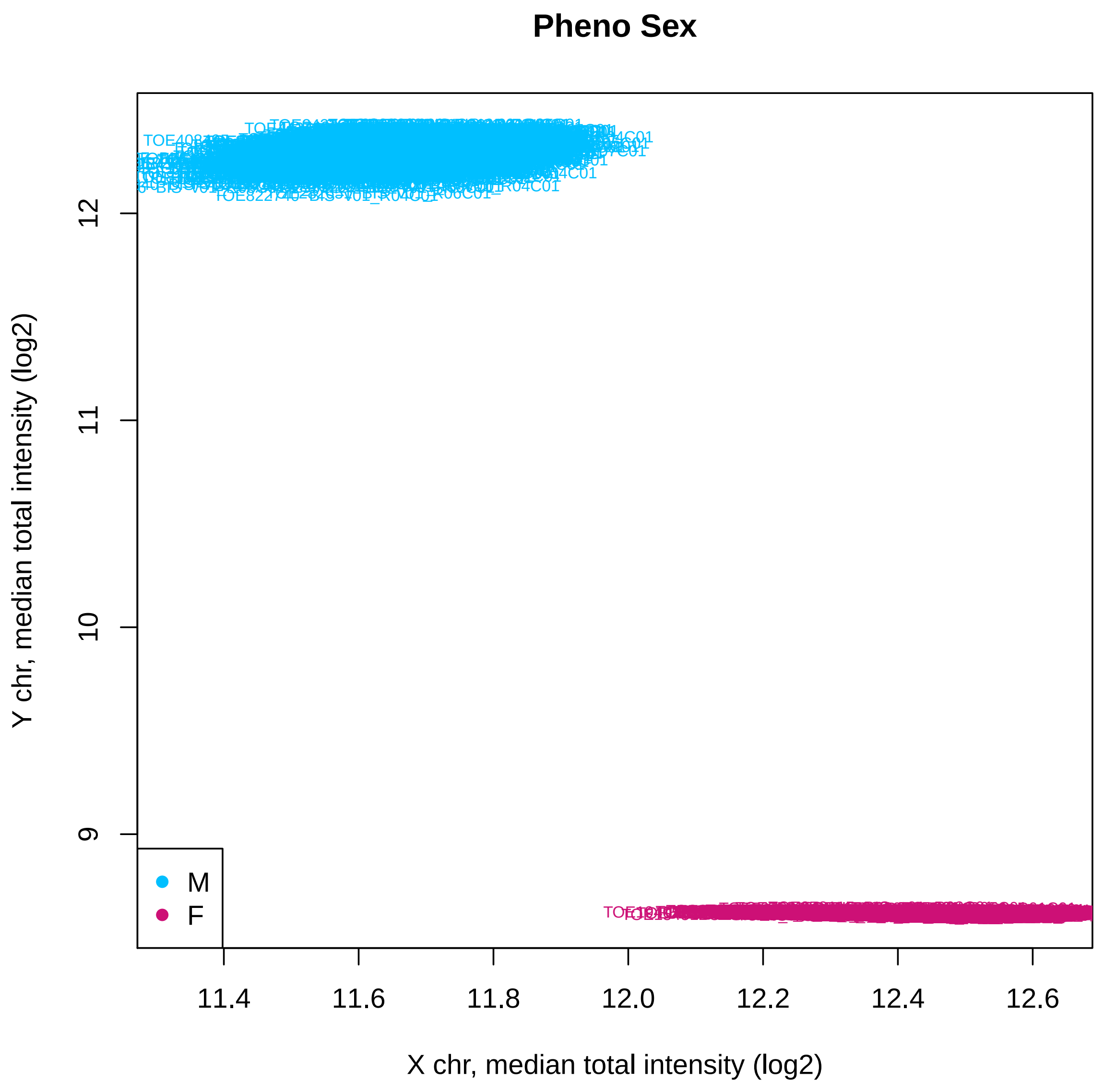
2.1 Failed probes loading

```
#############################
# CAMP funnorm-normalized mset
#############################
load(file=file.path(results.dir, "mset.camp.funnorm_hg19_1620502108.RData"))

#############################
# Failed probes based on detP
# see QC code for details
#############################
load(file=file.path(results.dir, "failedProbes_CAMP_hg19_1620502108.RData"))
length(failedProbes)

## [1] 7208

betas <- getBeta(mset.camp.funnorm)
ann850k <- getAnnotation(mset.camp.funnorm)
pData.camp <- pData(mset.camp.funnorm)
```

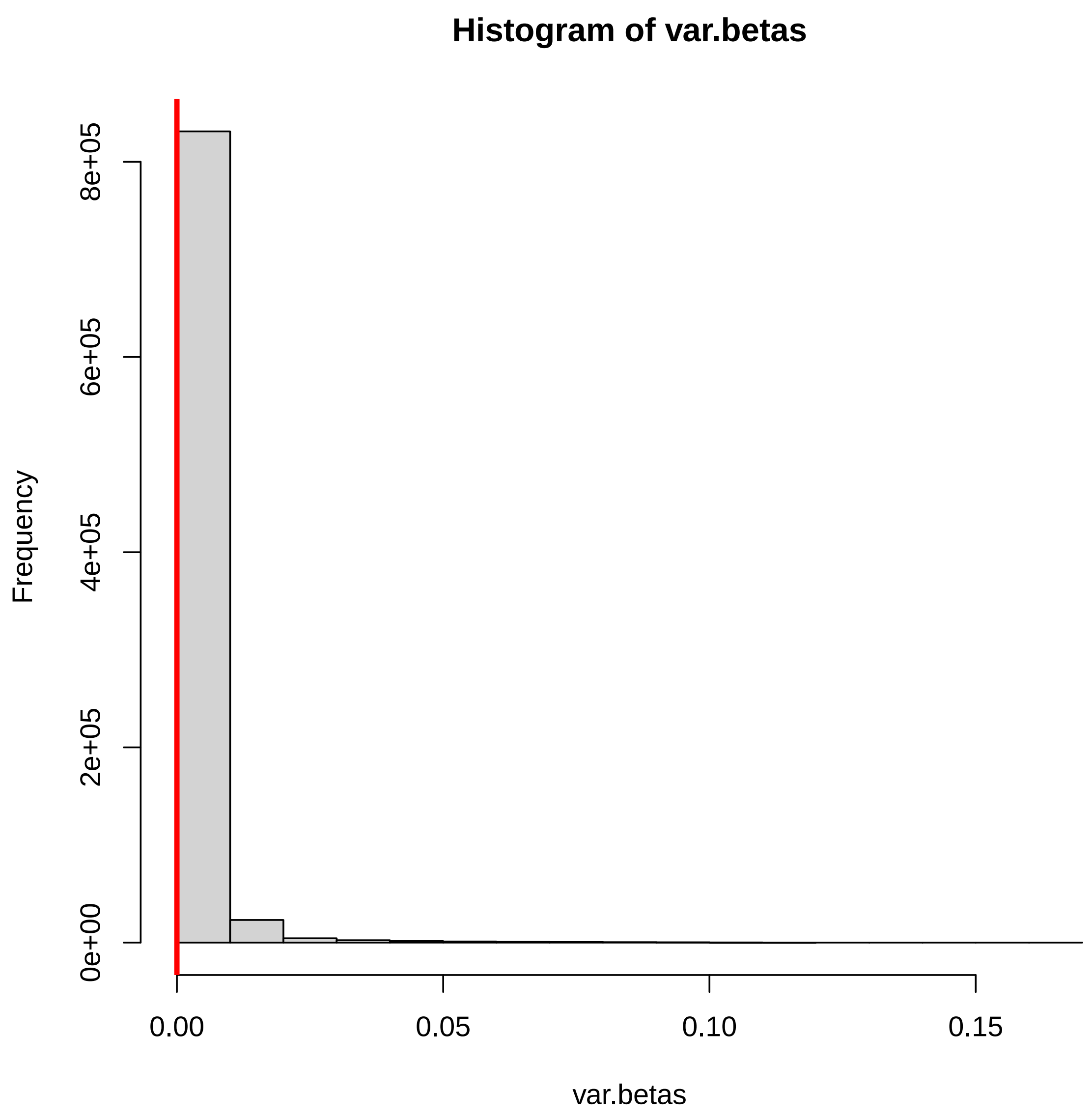
2.2 Probe level cleaning and rcp

```
########################
# Probe filtering stats
########################

##########################################
# Failed probes identified using meffil
# not using them though, just to stay
# within the minfi framework for this
##########################################

fail.cgs <- read.table(file=file.path(meff.dir, "qc/camp_failed_cgs_hg19_1618342534.txt"),
                       sep="\t", header=T,stringsAsFactors=FALSE)
fail.cgs <- fail.cgs$x
length(fail.cgs)

## [1] 5697

length(intersect(failedProbes, fail.cgs))

## [1] 5649

# both sex chromosomes
xychr = (featureNames(mset.camp.funnorm) %in% ann850k$Name[ann850k$chr %in% c("chrX","chrY")])
table(xychr)

## xychr
##  FALSE   TRUE
## 846232  19627

auto = !(featureNames(mset.camp.funnorm) %in% ann850k$Name[ann850k$chr %in% c("chrX","chrY")])
mset.auto = mset.camp.funnorm[auto,]
auto.probes <- featureNames(mset.auto)
length(auto.probes) # used later to extract betas from autosomes

## [1] 846232

rm(mset.auto) # to clear out memory

# count sex chromosomes individually
dim(ann850k[ann850k$chr=="chrX",])

## [1] 19090    46

dim(ann850k[ann850k$chr=="chrY",])

## [1] 537  46

#Gender check plot using median total intensities X and Y chr
# predictedSex <- getSex(mset.camp.funnorm, cutoff = -2)$predictedSex
xy <- getSex(mset.camp.funnorm, cutoff = -2)
xy$sex <- pData.camp$Gender
head(xy)

## DataFrame with 6 rows and 4 columns
##                               xMed      yMed predictedSex         sex
##                          <numeric> <numeric>  <character> <character>
## TOE654293-BIS-v01_R04C01   11.8223  12.32119            M           M
## TOE309577-BIS-v01_R04C01   11.8706  12.36684            M           M
## TOE536344-BIS-v01_R02C01   12.3718   8.62438            F           F
## TOE939881-BIS-v01_R05C01   11.6358  12.30322            M           M
## TOE840792-BIS-v01_R04C01   12.4004   8.62056            F           F
## TOE501225-BIS-v01_R06C01   11.4953  12.17798            M           M
```

```
table(xy$sex, xy$predictedSex) # should be same

##
##       F   M
##   F 675   0
##   M   0 832

# Plots based on phenotype sex
plot(xy$xMed, xy$yMed, type = "n", main="Pheno Sex",
     xlab = "X chr, median total intensity (log2)",
     ylab = "Y chr, median total intensity (log2)")
id <- rownames(xy)
colors=c("deeppink3","deepskyblue")
text(xy$xMed, xy$yMed, id, col=colors[as.factor(xy$sex)], cex=0.6)
legend("bottomleft", c("M", "F"),
       col = c("deepskyblue", "deeppink3"), pch = 16)
```



```
# there shouldn't be any sex mismatches at this stage
pdf(file=file.path(plots.dir, "gender_check_xy_sex_CAMP.pdf"),
    width = 5, height = 5)
plot(xy$xMed, xy$yMed, type = "n", main="Pheno Sex",
     xlab = "X chr, median total intensity (log2)",
     ylab = "Y chr, median total intensity (log2)")
id <- rownames(xy)
colors=c("deeppink3","deepskyblue")
text(xy$xMed, xy$yMed, id, col=colors[as.factor(xy$sex)], cex=0.6)
legend("bottomleft", c("M", "F"),
       col = c("deepskyblue", "deeppink3"), pch = 16)
dev.off()

## pdf
##   2

################################
# Minimum variance pruning (just checking)
################################
var.betas <- rowVars(betas)
cutoff <- quantile(var.betas,0.01, na.rm=TRUE)
print(table(var.betas > cutoff))

##
##  FALSE   TRUE
##   8659 857200

hist(var.betas)
abline(v=cutoff,col='red',lwd=3)
```



```
#betas.use <- betas[var.betas > cutoff,]
#dim(betas.use)
##########################################

# cross reactive probes and CH/rs probes
crossprobes <- cross_probes$sample
ch <- grep("^ch.", rownames(ann850k), value=TRUE); length(ch)

## [1] 2932

rs <- grep("^rs", rownames(ann850k), value=TRUE); length(rs)

## [1] 0

# probes with SNPs at the single base extension (minor allele frequency (MAF) >5%), probes containing
cpg.snpsUP <- LociWithSnps(mset.camp.funnorm, snps=c("SBE","CpG"), maf=0.05)
dim(cpg.snpsUP);head(cpg.snpsUP)

## [1] 11681     7
## DataFrame with 6 rows and 7 columns
##                Probe_rs Probe_maf      CpG_rs    CpG_maf      SBE_rs    SBE_maf
##             <character> <numeric> <character> <numeric> <character> <numeric>
## cg09139287          NA         NA   rs2905055  0.336368   rs2905055  0.336368
## cg05321646          NA         NA  rs74714520  0.428571  rs74714520  0.428571
## cg13692836          NA         NA  rs13303328  0.145985          NA        NA
## cg06624358          NA         NA  rs56024075  0.070023          NA        NA
## cg10644916          NA         NA   rs3813184  0.087352   rs3813184  0.087352
## cg10625579          NA         NA  rs76233940  0.066406  rs76233940  0.066406
##                 rownos
##              <integer>
## cg09139287         103
## cg05321646         133
## cg13692836         208
## cg06624358         210
## cg10644916         288
## cg10625579         380
```

```
save(cpg.snpsUP, file=file.path(results.dir,
            paste0("cpg_snpsUP_", timeStamp,".RData")))

cpg.snpsUP <- rownames(cpg.snpsUP)
length(cpg.snpsUP)

## [1] 11681

# just checking stats for 2 of the SUPs
summary(betas["cg09139287",])

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.02802 0.29311 0.37724 0.42118 0.54218 0.90309

summary(betas["cg05321646",])

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.5970  0.7402  0.7683  0.7686  0.7972  0.9093

rm(mset.camp.funnorm) # clear memory, would not need this further in the code

##############################################
# Probe filtering-cleaning/setting to missing
##############################################

dim(betas)

## [1] 865859   1507

betas[(rownames(betas) %in% cpg.snpsUP),] <- NA
# gives an idea about how many probes set to missing at each step
dim(na.omit(betas))

## [1] 854178   1507

# detP>0.01 threshold in more than 20% of the samples
betas[(rownames(betas) %in% failedProbes),] <- NA
dim(na.omit(betas))

## [1] 847350   1507

betas[(rownames(betas) %in% crossprobes),] <- NA
dim(na.omit(betas))

## [1] 804105   1507
```

```
betas[(rownames(betas) %in% ch),] <- NA
dim(na.omit(betas))
```

```
## [1] 802843   1507
```

```
betas[(rownames(betas) %in% rs),] <- NA
dim(na.omit(betas))
```

```
## [1] 802843   1507
```

```
##############################
# RCP on noob normalized and
# cleaned betas
##############################
dim(betas)
```

```
## [1] 865859   1507
```

```
dim(ann850k)
```

```
## [1] 865859     46
```

```
norm.betas.rcp <- rcp.mod(betas, ann850k)
```

```
######################################################################
# Normalized betas including parents and probands and all chromosomes
######################################################################
save(norm.betas.rcp, ann850k, file=file.path(results.dir,
            paste0("norm.betas.camp_rcp_hg19_clean_allchr_", timeStamp,".RData")))

# frequency distribution plots for funnorm betas before RCP
# again this takes a while so not printing in report, but saving it
beta1=betas[ann850k$Type=="I",]
beta2=betas[ann850k$Type=="II",]

jpeg(file = file.path(plots.dir, "freq_distribution_norm_betas_CAMP.jpg"),
    width = 750, height = 1500)
#jpeg("distributions_CAMP.jpg",height=900,width=500)
par(mfrow=c(3,1))
multifreqpoly(betas,main="Multifreqpoly",xlab="Beta value")
multifreqpoly(beta1,main="Multifreqpoly: Infinium I", xlab="Beta value")
multifreqpoly(beta2,main="Multifreqpoly: Infinium II", xlab="Beta value")
dev.off()
```

```
## pdf
##   2
```

```
# frequency distribution plots for funnorm betas after RCP
beta1=norm.betas.rcp[ann850k$Type=="I",]
beta2=norm.betas.rcp[ann850k$Type=="II",]

jpeg(file = file.path(plots.dir, "freq_distribution_norm_betas_rcp_CAMP.jpg"),
    width = 750, height = 1500)
par(mfrow=c(3,1))
multifreqpoly(norm.betas.rcp,main="Multifreqpoly",xlab="Beta value")
multifreqpoly(beta1,main="Multifreqpoly: Infinium I", xlab="Beta value")
multifreqpoly(beta2,main="Multifreqpoly: Infinium II", xlab="Beta value")
dev.off()
```

```
## pdf
##   2
```

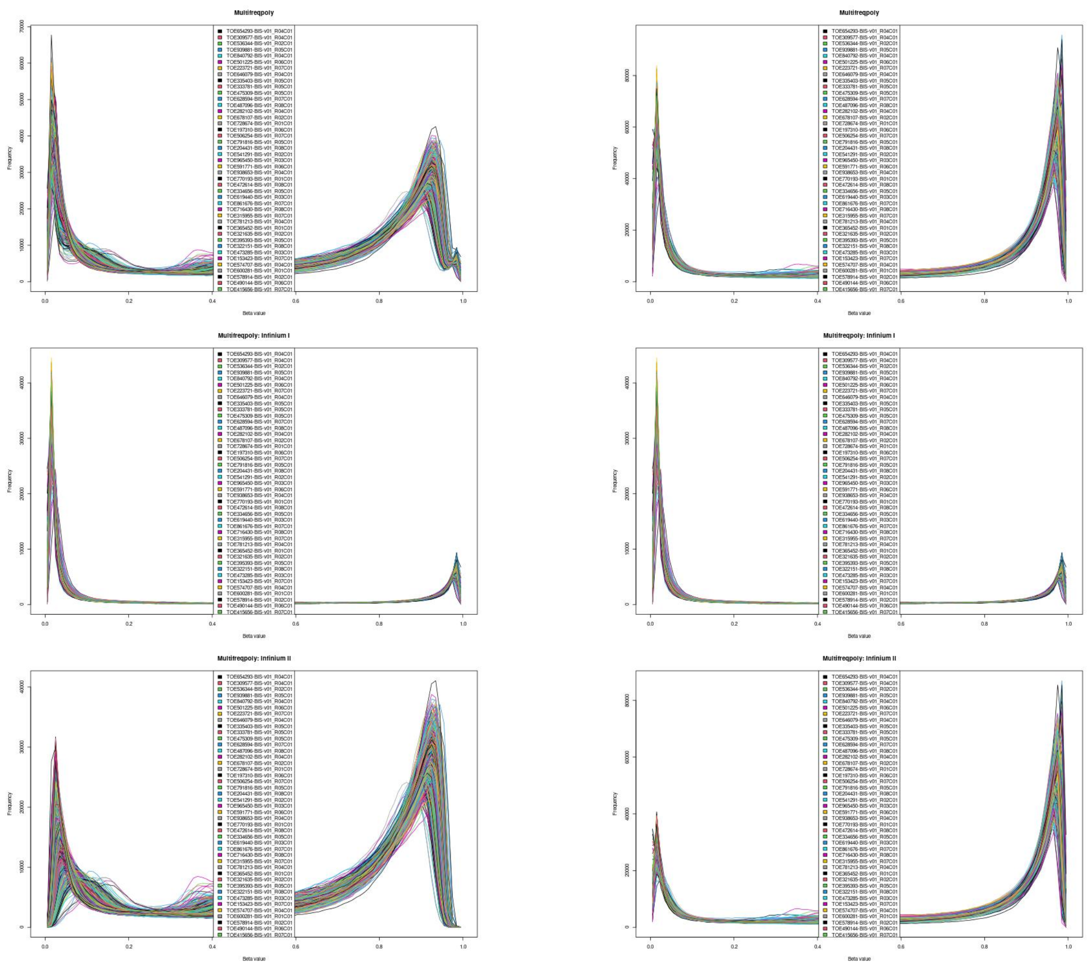
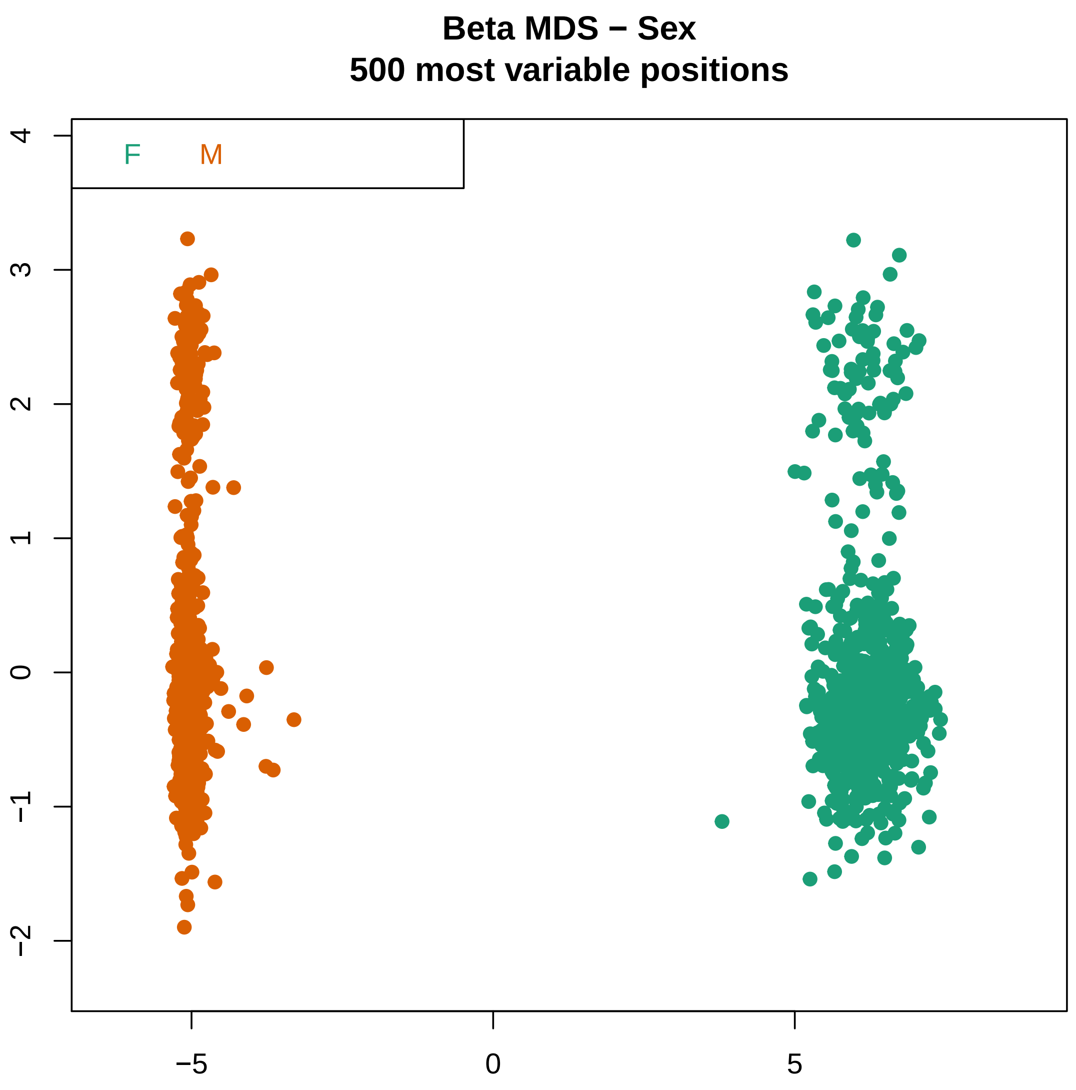


Figure 1: a) Normalized Distribution before rcp b) Normalized Distribution after rcp

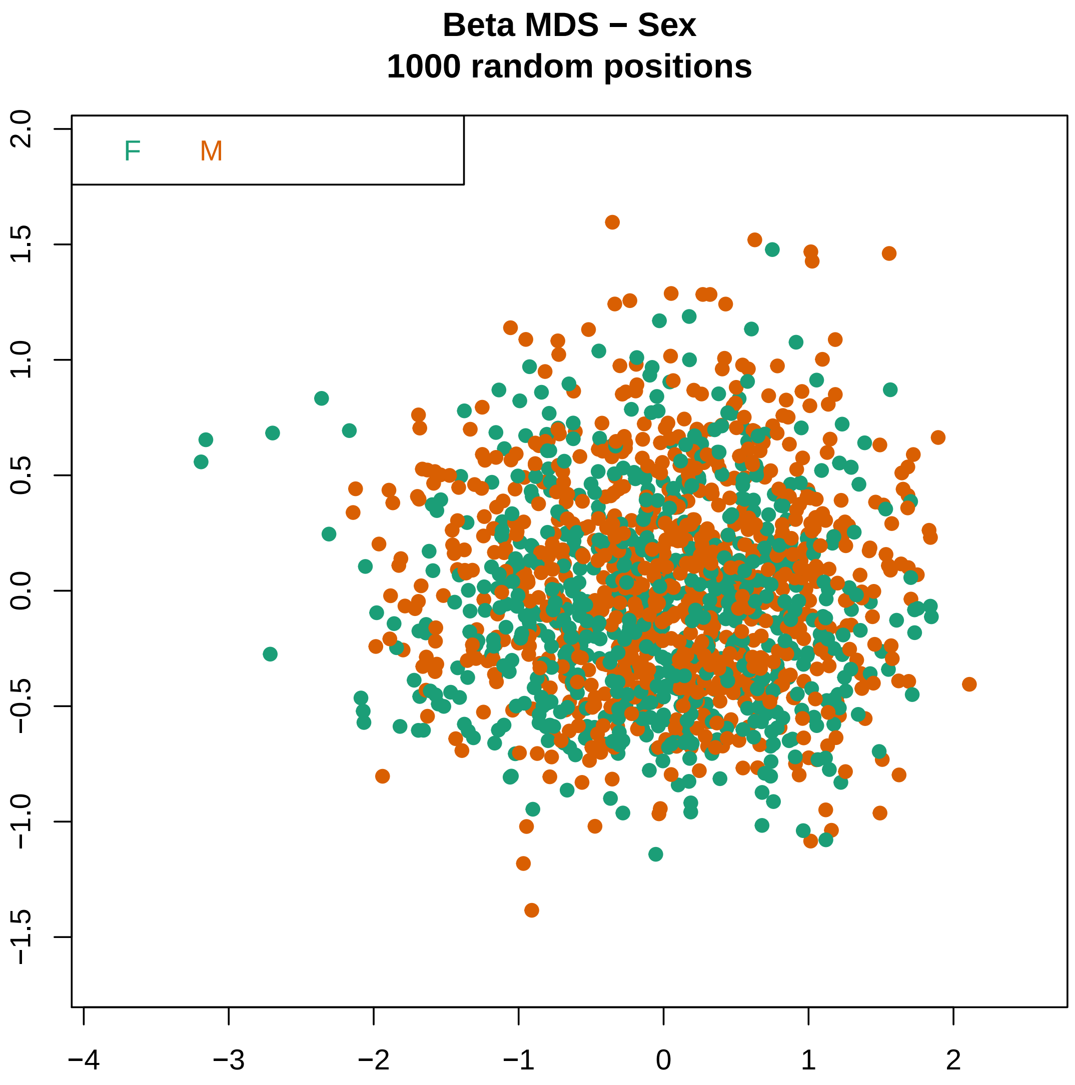
2.3 Beta to m-value conversion

```
##################
# Beta to M values
##################
rm(betas) # clearing some memory
mvals <- beta2m(norm.betas.rcp)
save(mvals, file=file.path(results.dir,paste0("norm.mvals.camp_hg19_clean_allchr_",
                                              timeStamp,".RData")))

head(pData.camp)

## DataFrame with 6 rows and 10 columns
##                                        Basename  S_SAMPLEID S_SUBJECTID
##                                     <character> <character> <character>
## TOE654293-BIS-v01_R04C01 LEVEL1/TOE654293-BIS.. S-000595596 ST-00065299
## TOE309577-BIS-v01_R04C01 LEVEL1/TOE309577-BIS.. S-000666101 ST-00039673
## TOE536344-BIS-v01_R02C01 LEVEL1/TOE536344-BIS.. S-000665199 ST-00035437
## TOE939881-BIS-v01_R05C01 LEVEL1/TOE939881-BIS.. S-000603292 ST-00063245
## TOE840792-BIS-v01_R04C01 LEVEL1/TOE840792-BIS.. S-000608860 ST-00040629
## TOE501225-BIS-v01_R06C01 LEVEL1/TOE501225-BIS.. S-000594629 ST-00042273
##                               Gender       TOEID   S_STUDYID
##                          <character> <character> <character>
## TOE654293-BIS-v01_R04C01           M   TOE654293       ABRIG
## TOE309577-BIS-v01_R04C01           M   TOE309577        CAMP
## TOE536344-BIS-v01_R02C01           F   TOE536344        CAMP
## TOE939881-BIS-v01_R05C01           M   TOE939881       ABRIG
## TOE840792-BIS-v01_R04C01           F   TOE840792        CAMP
## TOE501225-BIS-v01_R06C01           M   TOE501225        CAMP
##                                       filenames      xMed      yMed
##                                     <character> <numeric> <numeric>
## TOE654293-BIS-v01_R04C01 LEVEL1/TOE654293-BIS..   11.8223  12.32119
## TOE309577-BIS-v01_R04C01 LEVEL1/TOE309577-BIS..   11.8706  12.36684
## TOE536344-BIS-v01_R02C01 LEVEL1/TOE536344-BIS..   12.3718   8.62438
## TOE939881-BIS-v01_R05C01 LEVEL1/TOE939881-BIS..   11.6358  12.30322
## TOE840792-BIS-v01_R04C01 LEVEL1/TOE840792-BIS..   12.4004   8.62056
## TOE501225-BIS-v01_R06C01 LEVEL1/TOE501225-BIS..   11.4953  12.17798
##                          predictedSex
##                           <character>
## TOE654293-BIS-v01_R04C01            M
## TOE309577-BIS-v01_R04C01            M
## TOE536344-BIS-v01_R02C01            F
## TOE939881-BIS-v01_R05C01            M
## TOE840792-BIS-v01_R04C01            F
## TOE501225-BIS-v01_R06C01            M

# checking the clustering
pdf(file = file.path(plots.dir, "MDS_sex_500pos.pdf"), width = 6, height = 6)
mdsPlot(as.matrix(norm.betas.rcp), numPositions=500,
        main=sprintf("Beta MDS - Sex\n%d most variable positions", 500),
        pch=19,  legendNCol=5, sampGroups=pData.camp$Gender,
        legendPos="topleft", pal=c(brewer.pal(8, "Dark2"),
                                   brewer.pal(12, "Paired")))
dev.off()

## pdf
##   2

# select 1000 rows at random and then plot instead of 500 most variable
betas.rand <- norm.betas.rcp[sample(nrow(norm.betas.rcp), 1000), ]
```

```
pdf(file = file.path(plots.dir, "MDS_sex_1000pos_rand.pdf"), width = 6, height = 6)
mdsPlot(as.matrix(betas.rand), numPositions=1000,
        main=sprintf("Beta MDS - Sex\n%d random positions", 1000),
        pch=19,  legendNCol=5, sampGroups=pData.camp$Gender,
        legendPos="topleft", pal=c(brewer.pal(8, "Dark2"),
                                   brewer.pal(12, "Paired")))
dev.off()

## pdf
##   2

mdsPlot(as.matrix(norm.betas.rcp), numPositions=500,
        main=sprintf("Beta MDS - Sex\n%d most variable positions", 500),
        pch=19,  legendNCol=5, sampGroups=pData.camp$Gender,
        legendPos="topleft", pal=c(brewer.pal(8, "Dark2"),
                                   brewer.pal(12, "Paired")))
```



```
mdsPlot(as.matrix(betas.rand), numPositions=1000,
        main=sprintf("Beta MDS - Sex\n%d random positions", 1000),
        pch=19,  legendNCol=5, sampGroups=pData.camp$Gender,
        legendPos="topleft", pal=c(brewer.pal(8, "Dark2"),
                                   brewer.pal(12, "Paired")))
```



3 PCAs on autosomes

```
dim(pDat.camp); dim(camp.pheno)

## Error in eval(expr, envir, enclos):  object 'pDat.camp' not found

## [1] 1041 1008

pData.camp$toe_ids <- rownames(pData.camp)
pData.pheno.camp <- merge(pData.camp, camp.pheno, by="S_SUBJECTID", sort=F)
dim(pData.pheno.camp)

## [1]  725 1018

norm.betas.rcp.prob <- norm.betas.rcp[,colnames(norm.betas.rcp) %in% pData.pheno.camp$toe_ids]
dim(norm.betas.rcp.prob)
```

```
## [1] 865859    725

#################################################################
# Normalized betas from probands and all chromosomes
# remove missing probes if needed before any downstream analysis
#################################################################

# number of probes remaining after removing missing/failed probes
dim(na.omit(norm.betas.rcp.prob))

## [1] 802682    725

save(norm.betas.rcp.prob,
     file=file.path(results.dir,paste0("norm.betas.camp_hg19_clean_allchr_probands_",
                                        timeStamp,".RData")))

rm(norm.betas.rcp.prob) # cleaning memory

# pca on autosomes
# autosomal.sites <- meffil.get.autosomal.sites("epic")
# length(autosomal.sites)
# autosomal.sites <- intersect(autosomal.sites, rownames(norm.betas.rcp))

norm.betas.rcp.auto <- norm.betas.rcp[rownames(norm.betas.rcp) %in% auto.probes,]
dim(norm.betas.rcp.auto)

## [1] 846232   1507

norm.betas.rcp.auto <- na.omit(norm.betas.rcp.auto)

norm.betas.rcp.auto.prob <- norm.betas.rcp.auto[,colnames(norm.betas.rcp.auto)
                                                %in% pData.pheno.camp$toe_ids]
dim(norm.betas.rcp.auto.prob)

## [1] 785352    725

rm(norm.betas.rcp)
rm(norm.betas.rcp.auto)

#################################################################
# this function will automatically save pcas in results directory
# Top  10  principal components can explain  how much data variation
#################################################################
pca.betas(norm.betas.rcp.auto.prob, n=10)

## Analysis is running, please wait...!
## Top  10  principal components can explain  36.20944 % of data
##     variation

#################################################################
# Normalized betas from probands and autosomes (no sex chr)
# removed missing probes removed as above for EWAS
#################################################################
save(norm.betas.rcp.auto.prob, file=file.path(results.dir,
                              paste0("norm.betas.camp_hg19_clean_NOsexchr_probands_",
                                     timeStamp,".RData")))
```

4 Session information

[1] "2021-05-12" [1] "2021-05-12 14:55:59 EDT"

- R version 4.0.3 (2020-10-10), `x86_64-pc-linux-gnu`
- Locale: `LC_CTYPE=en_US.UTF-8`, `LC_NUMERIC=C`, `LC_TIME=en_US.UTF-8`, `LC_COLLATE=en_US.UTF-8`, `LC_MONETARY=en_US.UTF-8`, `LC_MESSAGES=en_US.UTF-8`, `LC_PAPER=en_US.UTF-8`, `LC_NAME=C`, `LC_ADDRESS=C`, `LC_TELEPHONE=C`, `LC_MEASUREMENT=en_US.UTF-8`, `LC_IDENTIFICATION=C`
- Running under: `CentOS Linux 7 (Core)`
- Matrix products: default
- BLAS: `/app/R-4.0.3@i86-rhel7.0/lib64/R/lib/libRblas.so`
- LAPACK: `/app/R-4.0.3@i86-rhel7.0/lib64/R/lib/libRlapack.so`
- Base packages: base, datasets, graphics, grDevices, methods, parallel, stats, stats4, utils
- Other packages: annotate 1.68.0, AnnotationDbi 1.52.0, Biobase 2.50.0, BiocGenerics 0.36.1, BiocParallel 1.24.1, Biostrings 2.58.0, bumphunter 1.32.0, Cairo 1.5-12.2, colorRamps 2.3, data.table 1.14.0, DNAcopy 1.64.0, doParallel 1.0.16, dplyr 1.0.3, e1071 1.7-6, ENmix 1.26.10, fastICA 1.2-2, FDb.InfiniumMethylation.hg19 2.2.0, forcats 0.5.1, foreach 1.5.1, gdsfmt 1.26.1, genefilter 1.72.1, geneplotter 1.68.0, GenomeInfoDb 1.26.7, GenomicFeatures 1.42.3, GenomicRanges 1.42.0, GGally 2.1.0, ggplot2 3.3.3, ggrepel 0.9.1, gplots 3.1.1, gridExtra 2.3, here 1.0.1, IlluminaHumanMethylation450kanno.ilmn12.hg19 0.6.0, IlluminaHumanMethylationEPICanno.ilm10b4.hg19 0.6.0, IlluminaHumanMethylationEPICmanifest 0.3.0, illuminaio 0.32.0, impute 1.64.0, IRanges 2.24.1, isva 1.9, iterators 1.0.13, JADE 2.0-3, knitr 1.33, lattice 0.20-44, limma 3.46.0, lme4 1.1-26, locfit 1.5-9.4, lumi 2.42.0, markdown 1.1, MASS 7.3-54, Matrix 1.3-3, MatrixGenerics 1.2.1, matrixStats 0.58.0, meffil 1.1.1, methylumi 2.36.0, mgcv 1.8-35, minfi 1.36.0, multcomp 1.4-17, mvtnorm 1.1-1, nlme 3.1-152, org.Hs.eg.db 3.12.0, plyr 1.8.6, preprocessCore 1.52.1, purrr 0.3.4, quadprog 1.5-8, qvalue 2.22.0, R.methodsS3 1.8.1, R.oo 1.24.0, R.utils 2.10.1, RColorBrewer 1.1-2, readr 1.4.0, reshape2 1.4.4, robustbase 0.93-7, ROC 1.66.0, RSpectra 0.16-0, S4Vectors 0.28.1, scales 1.1.1, SmartSVA 0.1.3, statmod 1.4.35, stringi 1.5.3, stringr 1.4.0, SummarizedExperiment 1.20.0, survival 3.2-11, sva 3.38.0, TH.data 1.0-10, tibble 3.1.1, tidyr 1.1.3, tidyverse 1.3.0, TxDb.Hsapiens.UCSC.hg19.knownGene 3.2.2, wateRmelon 1.34.0, XML 3.99-0.6, XVector 0.30.0
- Loaded via a namespace (and not attached): affy 1.68.0, affyio 1.60.0, AnnotationHub 2.22.1, askpass 1.1, assertthat 0.2.1, backports 1.2.1, base64 2.0, beanplot 1.2, BiocFileCache 1.14.0, BiocManager 1.30.12, BiocVersion 3.12.0, biomaRt 2.46.3, bit 4.0.4, bit64 4.0.5, bitops 1.0-7, blob 1.2.1, boot 1.3-28, broom 0.7.6, cachem 1.0.4, caTools 1.18.2, cellranger 1.1.0, class 7.3-19, cli 2.5.0, clue 0.3-59, cluster 2.1.2, codetools 0.2-18, colorspace 2.0-1, compiler 4.0.3, crayon 1.4.1, curl 4.3.1, DBI 1.1.1, dbplyr 2.1.0, DelayedArray 0.16.3, DelayedMatrixStats 1.12.3, DEoptimR 1.0-8, digest 0.6.27, doRNG 1.8.2, dynamicTreeCut 1.63-1, edgeR 3.32.1, ellipsis 0.3.2, evaluate 0.14, ExperimentHub 1.16.1, fansi 0.4.2, fastmap 1.1.0, fs 1.5.0, generics 0.1.0, GenomeInfoDbData 1.2.4, GenomicAlignments 1.26.0, GEOquery 2.58.0, glue 1.4.2, grid 4.0.3, gtable 0.3.0, gtools 3.8.2, haven 2.4.1, HDF5Array 1.18.1, highr 0.9, hms 1.0.0, htmltools 0.5.1.1, httpuv 1.6.0, httr 1.4.2, interactiveDisplayBase 1.28.0, irr 0.84.1, jsonlite 1.7.2, KernSmooth 2.23-20, later 1.2.0, lifecycle 0.2.0, lpSolve 5.6.15, lubridate 1.7.10, magrittr 2.0.1, mclust 5.4.7, memoise 2.0.0, mime 0.10, minqa 1.2.4, modelr 0.1.8, multtest 2.46.0, munsell 0.5.0, nleqslv 3.3.2, nloptr 1.2.2.2, nor1mix 1.3-0, openssl 1.4.4, pillar 1.6.0, pkgconfig 2.0.3, prettyunits 1.1.1, progress 1.2.2, promises 1.2.0.1, proxy 0.4-25, ps 1.6.0, R6 2.5.0, rappdirs 0.3.3, Rcpp 1.0.6, RCurl 1.98-1.3, readxl 1.3.1, reprex 2.0.0, reshape 0.8.8, rhdf5 2.34.0, rhdf5filters 1.2.1, Rhdf5lib 1.12.1, rlang 0.4.9, rngtools 1.5, RPMM 1.25, rprojroot 2.0.2, Rsamtools 2.6.0, RSQLite 2.2.3, rstudioapi 0.13, rtracklayer 1.50.0, rvest 0.3.6, sandwich 3.0-0, scrime 1.3.5, shiny 1.6.0, siggenes 1.64.0, sparseMatrixStats 1.2.1, splines 4.0.3, tidyselect 1.1.1, tools 4.0.3, utf8 1.2.1, vctrs 0.3.6, withr 2.4.2, xfun 0.22, xml2 1.3.2, xtable 1.8-4, yaml 2.2.1, zlibbioc 1.36.0, zoo 1.8-9