

main

September 14, 2021

1 eQTL boxplot

This is script ported from python to fix unknown plotting error.

```
[1]: suppressPackageStartupMessages({  
      library(tidyverse)  
      library(ggpubr)  
    })
```

1.1 Functions

```
[2]: feature = "genes"  
      tissue = "Caudate"
```

1.1.1 Cached functions

```
[3]: get_residualized_df <- function(){  
      expr_file = "../_m/genes_residualized_expression.csv"  
      return(data.table::fread(expr_file) %>% column_to_rownames("gene_id"))  
    }  
    memRES <- memoise::memoise(get_residualized_df)  
  
    get_biomart_df <- function(){  
      biomart = data.table::fread("../_h/biomart.csv")  
    }  
    memMART <- memoise::memoise(get_biomart_df)  
  
    get_pheno_df <- function(){  
      phenotype_file = paste0('/ceph/projects/v4_phase3_paper/inputs/',  
                              'phenotypes/_m/merged_phenotypes.csv')  
      return(data.table::fread(phenotype_file))  
    }  
    memPHENO <- memoise::memoise(get_pheno_df)  
  
    get_tissue_eqtls <- function(){  
      mashr_file = paste0("../_m/mashr/summary_table/_m/",  
                          "BrainSeq_sexGenotypes_4features_3regions_pgc2.txt.gz")  
      return(data.table::fread(mashr_file) %>%
```

```

        filter(Type == "Gene", Tissue == "Caudate") %>%
        select(gene_id, variant_id, lfsr))
}
memTISSUE <- memoise::memoise(get_tissue_eqtls)

get_eqtl_df <- function(){
  fastqtl_file = paste0("../.../prep_eqtl_analysis/", tolower(tissue),
                        "/genes/prepare_expression/fastqtl_nominal/",
                        "multiple_corrections/_m/Brainseq_LIBD.txt.gz")
  eqtl_df = data.table::fread(fastqtl_file) %>%
    filter(gene_id %in% unique(memTISSUE())$gene_id) %>%
    arrange(BF)
  return(eqtl_df)
}
memEQTL <- memoise::memoise(get_eqtl_df)

get_genotypes <- function(){
  traw_file = paste0("/ceph/projects/brainseq/genotype/download/topmed/
  ↪convert2plink/",
                    "filter_maf_01/a_transpose/_m/LIBD_Brain_TopMed.traw")
  traw = data.table::fread(traw_file) %>% rename_with(~ gsub('\\_.*', '', .x))
  return(traw)
}
memSNPs <- memoise::memoise(get_genotypes)

get_snp_df <- function(variant_id, gene_id){
  zz = get_genotype_annot() %>% filter(SNP == variant_id)
  xx = get_snps_df() %>% filter(SNP == variant_id) %>%
    column_to_rownames("SNP") %>% t %>% as.data.frame %>%
    rownames_to_column("BrNum") %>% mutate(COUNTED=zz$COUNTED, ALT=zz$ALT)
  ↪%>%
    rename("SNP"=all_of(variant_id))
  yy = memRES()[gene_id, ] %>% t %>% as.data.frame %>%
    rownames_to_column("RNum") %>% inner_join(memPHENO(), by="RNum")
  ## Annotated SNPs
  letters = c()
  for(ii in seq_along(xx$COUNTED)){
    a0 = xx$COUNTED[ii]; a1 = xx$ALT[ii]; number = xx$SNP[ii]
    letters <- append(letters, letter_snp(number, a0, a1))
  }
  xx = xx %>% mutate(LETTER=letters, ID=paste(SNP, LETTER, sep="\n"))
  df = inner_join(xx, yy, by="BrNum") %>% mutate_if(is.character, as.factor)
  return(df)
}
memDF <- memoise::memoise(get_snp_df)

```

1.1.2 Simple functions

```
[4]: get_genotype_annot <- function(){
      return(memSNPs() %>% select(CHR, SNP, POS, COUNTED, ALT))
    }

get_snps_df <- function(){
  return(memSNPs() %>% select("SNP", starts_with("Br")))
}

letter_snp <- function(number, a0, a1){
  if(is.na(number)){ return(NA) }
  if( length(a0) == 1 & length(a1) == 1){
    seps = ""; collapse=""
  } else {
    seps = " "; collapse=NULL
  }
  return(paste(paste0(rep(a0, number), collapse = collapse),
               paste0(rep(a1, (2-number)), collapse = collapse), sep=seps))
}

save_ggplots <- function(fn, p, w, h){
  for(ext in c('.pdf', '.png', '.svg')){
    ggsave(paste0(fn, ext), plot=p, width=w, height=h)
  }
}

get_gene_symbol <- function(gene_id){
  ensemblID = gsub("\\..*", "", gene_id)
  geneid = memMART() %>% filter(ensembl_gene_id == gsub("\\..*", "", gene_id))
  if(dim(geneid)[1] == 0){
    return("")
  } else {
    return(geneid$external_gene_name)
  }
}

plot_simple_eqtl <- function(fn, gene_id, variant_id, eqtl_annot){
  bxp = memDF(variant_id, gene_id) %>%
    ggboxplot(x="ID", y=gene_id, fill="Sex", color="Sex", add="jitter",
              facet.by="Region", panel.labs.font=list(face='bold'),
              xlab=variant_id, ylab="Residualized Expression", outlier.
  ↪ shape=NA,
              add.params=list(alpha=0.5), alpha=0.4, legend="bottom",
              palette="npg", ggtheme=theme_pubr(base_size=20, border=TRUE))
  ↪ +
  font("xy.title", face="bold") +

```

```

    ggtitle(paste(get_gene_symbol(gene_id), gene_id, eqtl_annot, sep='\n'))
  }
  theme(plot.title = element_text(hjust = 0.5, face="bold"))
  print(bxp)
  save_ggplots(fn, bxp, 10, 7)
}

```

1.1.3 GWAS plots

```

[5]: get_gwas_snps <- function(){
  gwas_snp_file = paste0('/ceph/projects/v4_phase3_paper/inputs/sz_gwas/
  pgc2_clozuk/',
                        'map_phase3/_m/libd_hg38_pgc2sz_snps_p5e_minus8.tsv')
  gwas_df = data.table::fread(gwas_snp_file) %>% arrange(P)
  return(gwas_df)
}
memGWAS <- memoise::memoise(get_gwas_snps)

get_gwas_snp <- function(variant){
  return(memGWAS() %>% filter(our_snp_id == variant))
}

get_risk_allele <- function(variant){
  gwas_snp = get_gwas_snp(variant)
  if(gwas_snp$OR > 1){
    ra = gwas_snp$A1
  }else{
    ra = gwas_snp$A2
  }
  return(ra)
}

get_eqtl_gwas_df <- function(){
  return(memTISSUE() %>% inner_join(memGWAS(),
  by=c("variant_id"="our_snp_id")))
}

get_gwas_ordered_snp_df <- function(variant_id, gene_id,
pgc2_a1_same_as_our_counted, OR){
  df = memDF(variant_id, gene_id)
  if(!pgc2_a1_same_as_our_counted){ # Fix bug with matching alleles!
    if(OR < 1){ df = df %>% mutate(SNP = 2-SNP, ID=paste(SNP, LETTER,
sep="\n")) }
  } else {
    if(OR > 1){ df = df %>% mutate(SNP = 2-SNP, ID=paste(SNP, LETTER,
sep="\n")) }
  }
}

```

```

    return(df)
}

plot_gwas_eqtl <- function(fn, gene_id, variant_id,
  ↪pgc2_a1_same_as_our_counted, OR, title){
  dt = get_gwas_ordered_snp_df(variant_id, gene_id,
  ↪pgc2_a1_same_as_our_counted, OR)
  y0 = quantile(dt[[gene_id]], probs=c(0.05))[[1]] - 0.26
  y1 = quantile(dt[[gene_id]], probs=c(0.95))[[1]] + 0.26
  bxp = dt %>% mutate_if(is.character, as.factor) %>%
    mutate(Region=gsub("HIPPO", "Hippocampus", Region)) %>%
    ggboxplot(x="ID", y=gene_id, fill="Sex", color="Sex", add="jitter",
      facet.by="Region", panel.labs.font=list(face='bold'),
      xlab=variant_id, ylab="Residualized Expression", outlier.
  ↪shape=NA,
      add.params=list(alpha=0.5), alpha=0.4, legend="bottom",
  ↪lims=c(y0,y1),
      palette="npg", ggtheme=theme_pubr(base_size=20, border=TRUE))
  ↪+
    font("xy.title", face="bold") + ggtitle(title) +
    theme(plot.title = element_text(hjust = 0.5, face="bold"))
  print(bxp)
  save_ggplots(fn, bxp, 10, 7)
}

```

1.2 Plot eQTL

1.2.1 Top 5 GWAS associated eQTLs

```

[6]: eqtl_gwas_df = get_eqtl_gwas_df() %>% group_by(gene_id) %>% arrange(lfsr) %>%
  slice(1) %>% inner_join(select(get_eqtl_df(), -variant_id),
  ↪by=c("gene_id")) %>%
  select(variant_id, gene_id, slope, BF, pgc2_a1_same_as_our_counted, OR, P)
eqtl_gwas_df

```

	variant_id <chr>	gene_id <chr>	slope <dbl>	BF <dbl>	pgc2_a1_same_a <lgl>
A grouped_df: 3 × 7	chr2:232928501:T:C	ENSG00000182600.9	0.424601	1.085450e-01	FALSE
	chr6:29688639:T:G	ENSG00000227262.3	0.499502	5.440699e-02	FALSE
	chr6:31867387:G:C	ENSG00000244731.7	-0.632753	7.852384e-05	FALSE

```

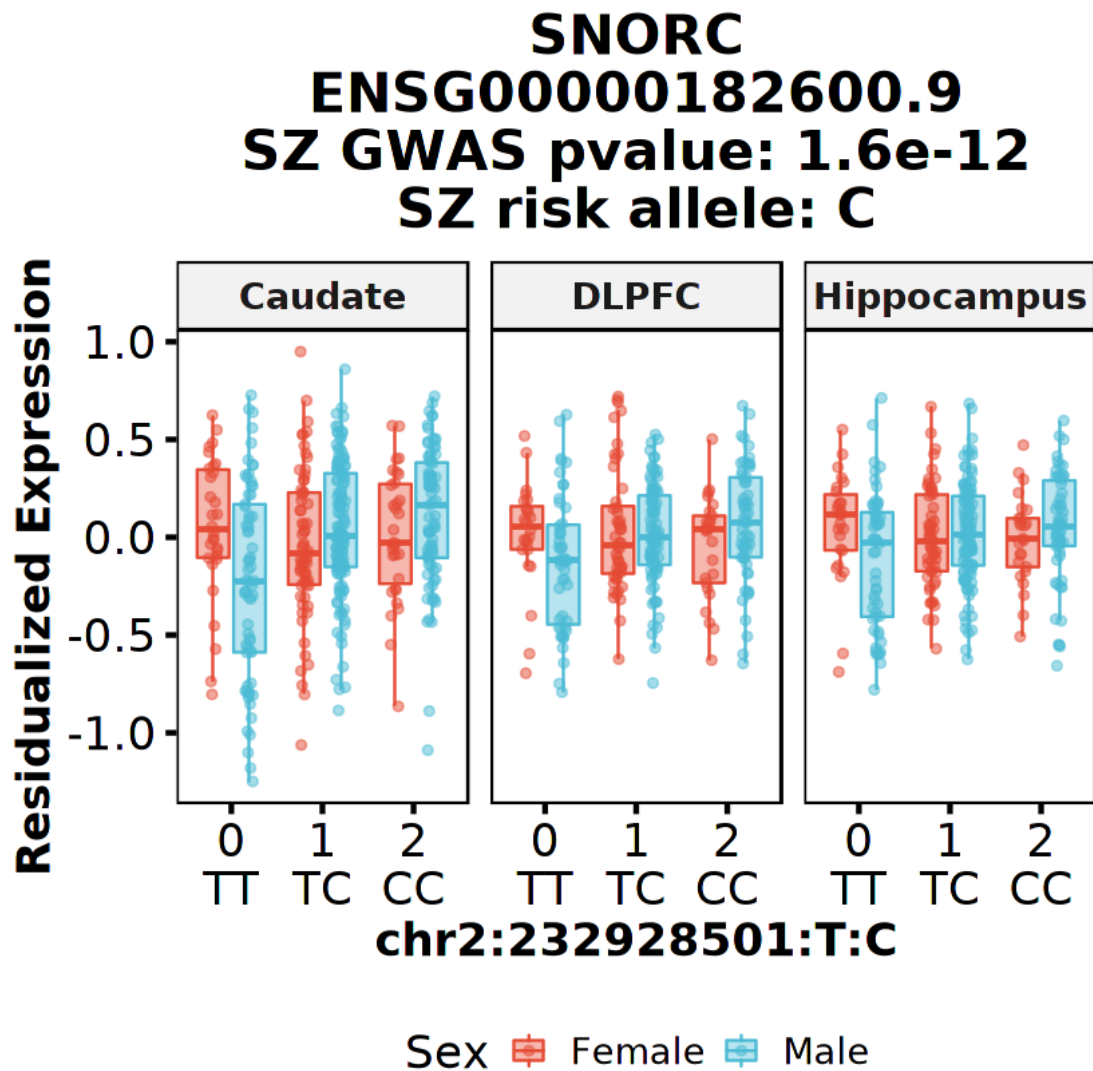
[7]: for(num in seq_along(eqtl_gwas_df$gene_id)){
  fn = paste("top",num,"interacting_eqtl_in_gwas_significant_snps", sep="_")
  variant_id = eqtl_gwas_df$variant_id[num]
  gene_id = eqtl_gwas_df$gene_id[num]
  pgc2_a1_same_as_our_counted = eqtl_gwas_df$pgc2_a1_same_as_our_counted[num]
  OR = eqtl_gwas_df$OR[num]
}

```

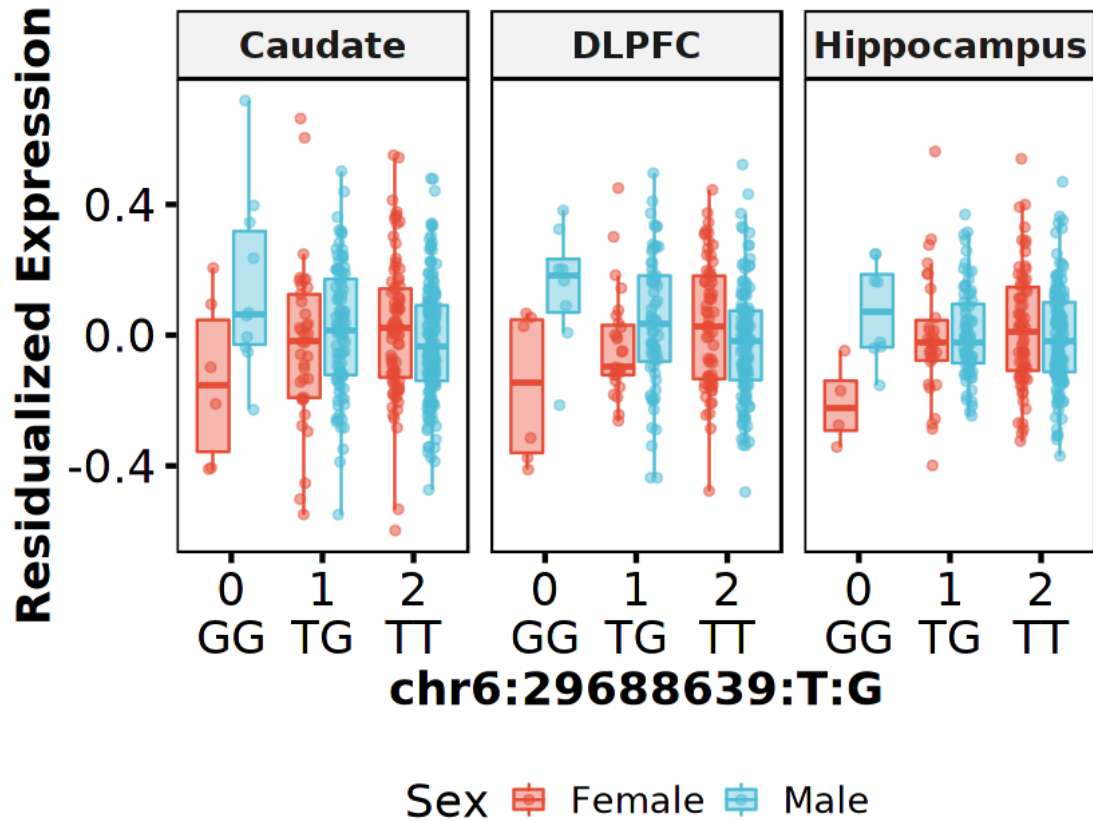
```

#eqtl_annot = paste("eQTL q-value:", signif(eqtl_gwas_df$BF[num], 2))
gwas_annot = paste("SZ GWAS pvalue:", signif(eqtl_gwas_df$P[num], 2))
risk_annot = paste("SZ risk allele:",
  ↪get_risk_allele(eqtl_gwas_df$variant_id[num]))
  title = paste(get_gene_symbol(gene_id), gene_id, gwas_annot, risk_annot,
  ↪sep='\n')
  plot_gwas_eqtl(fn, gene_id, variant_id, pgc2_a1_same_as_our_counted, OR,
  ↪title)
}

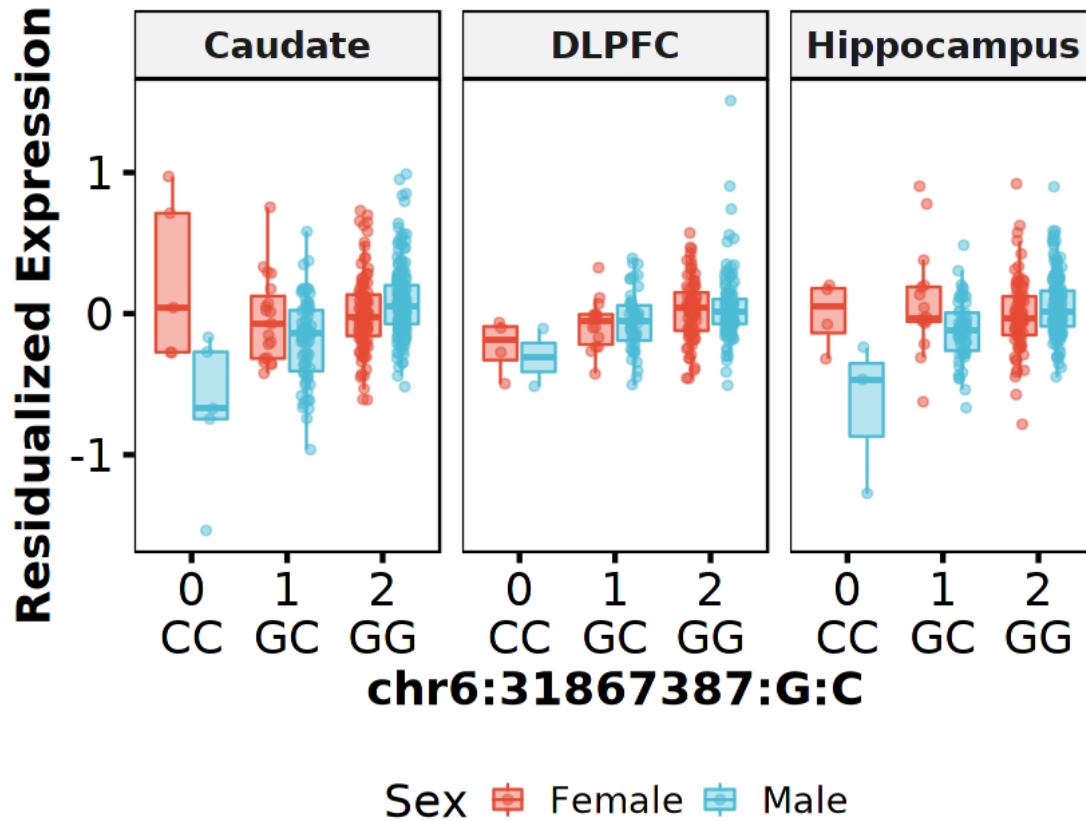
```



HCG4B
ENSG00000227262.3
SZ GWAS pvalue: 6.9e-15
SZ risk allele: T



C4A
ENSG00000244731.7
SZ GWAS pvalue: 1.1e-29
SZ risk allele: G



1.3 Session Info

```
[8]: Sys.time()
proc.time()
options(width = 120)
sessioninfo::session_info()
```

```
[1] "2021-09-14 15:31:46 EDT"
```

```
      user  system elapsed
1247.496  203.687   253.504
```

```
Session info
setting  value
```



```

version R version 4.0.3 (2020-10-10)
os      Arch Linux
system  x86_64, linux-gnu
ui      X11
language (EN)
collate en_US.UTF-8
ctype   en_US.UTF-8
tz      America/New_York
date    2021-09-14

```

Packages

package	* version	date	lib	source
abind	1.4-5	2016-07-21	[1]	CRAN (R 4.0.2)
assertthat	0.2.1	2019-03-21	[1]	CRAN (R 4.0.2)
backports	1.2.1	2020-12-09	[1]	CRAN (R 4.0.2)
base64enc	0.1-3	2015-07-28	[1]	CRAN (R 4.0.2)
broom	0.7.9	2021-07-27	[1]	CRAN (R 4.0.3)
cachem	1.0.6	2021-08-19	[1]	CRAN (R 4.0.3)
Cairo	1.5-12.2	2020-07-07	[1]	CRAN (R 4.0.2)
car	3.0-11	2021-06-27	[1]	CRAN (R 4.0.3)
carData	3.0-4	2020-05-22	[1]	CRAN (R 4.0.2)
cellranger	1.1.0	2016-07-27	[1]	CRAN (R 4.0.2)
cli	3.0.1	2021-07-17	[1]	CRAN (R 4.0.3)
colorspace	2.0-2	2021-06-24	[1]	CRAN (R 4.0.3)
crayon	1.4.1	2021-02-08	[1]	CRAN (R 4.0.3)
curl	4.3.2	2021-06-23	[1]	CRAN (R 4.0.3)
data.table	1.14.0	2021-02-21	[1]	CRAN (R 4.0.3)
DBI	1.1.1	2021-01-15	[1]	CRAN (R 4.0.2)
dbplyr	2.1.1	2021-04-06	[1]	CRAN (R 4.0.3)
digest	0.6.27	2020-10-24	[1]	CRAN (R 4.0.2)
dplyr	* 1.0.7	2021-06-18	[1]	CRAN (R 4.0.3)
ellipsis	0.3.2	2021-04-29	[1]	CRAN (R 4.0.3)
evaluate	0.14	2019-05-28	[1]	CRAN (R 4.0.2)
fansi	0.5.0	2021-05-25	[1]	CRAN (R 4.0.3)
farver	2.1.0	2021-02-28	[1]	CRAN (R 4.0.3)
fastmap	1.1.0	2021-01-25	[1]	CRAN (R 4.0.2)
forcats	* 0.5.1	2021-01-27	[1]	CRAN (R 4.0.2)
foreign	0.8-80	2020-05-24	[2]	CRAN (R 4.0.3)
fs	1.5.0	2020-07-31	[1]	CRAN (R 4.0.2)
generics	0.1.0	2020-10-31	[1]	CRAN (R 4.0.2)
ggplot2	* 3.3.5	2021-06-25	[1]	CRAN (R 4.0.3)
ggpubr	* 0.4.0	2020-06-27	[1]	CRAN (R 4.0.2)
ggsci	2.9	2018-05-14	[1]	CRAN (R 4.0.2)
ggsignif	0.6.2	2021-06-14	[1]	CRAN (R 4.0.3)
glue	1.4.2	2020-08-27	[1]	CRAN (R 4.0.2)
gtable	0.3.0	2019-03-25	[1]	CRAN (R 4.0.2)
haven	2.4.3	2021-08-04	[1]	CRAN (R 4.0.3)
hms	1.1.0	2021-05-17	[1]	CRAN (R 4.0.3)

htmltools	0.5.2	2021-08-25	[1]	CRAN	(R 4.0.3)
httr	1.4.2	2020-07-20	[1]	CRAN	(R 4.0.2)
IRdisplay	1.0	2021-01-20	[1]	CRAN	(R 4.0.2)
IRkernel	1.2	2021-05-11	[1]	CRAN	(R 4.0.3)
jsonlite	1.7.2	2020-12-09	[1]	CRAN	(R 4.0.2)
labeling	0.4.2	2020-10-20	[1]	CRAN	(R 4.0.2)
lifecycle	1.0.0	2021-02-15	[1]	CRAN	(R 4.0.3)
lubridate	1.7.10	2021-02-26	[1]	CRAN	(R 4.0.3)
magrittr	2.0.1	2020-11-17	[1]	CRAN	(R 4.0.2)
memoise	2.0.0	2021-01-26	[1]	CRAN	(R 4.0.2)
modelr	0.1.8	2020-05-19	[1]	CRAN	(R 4.0.2)
munsell	0.5.0	2018-06-12	[1]	CRAN	(R 4.0.2)
openxlsx	4.2.4	2021-06-16	[1]	CRAN	(R 4.0.3)
pbdZMQ	0.3-5	2021-02-10	[1]	CRAN	(R 4.0.3)
pillar	1.6.2	2021-07-29	[1]	CRAN	(R 4.0.3)
pkgconfig	2.0.3	2019-09-22	[1]	CRAN	(R 4.0.2)
purrr	* 0.3.4	2020-04-17	[1]	CRAN	(R 4.0.2)
R.methodsS3	1.8.1	2020-08-26	[1]	CRAN	(R 4.0.3)
R.oo	1.24.0	2020-08-26	[1]	CRAN	(R 4.0.3)
R.utils	2.10.1	2020-08-26	[1]	CRAN	(R 4.0.3)
R6	2.5.1	2021-08-19	[1]	CRAN	(R 4.0.3)
Rcpp	1.0.7	2021-07-07	[1]	CRAN	(R 4.0.3)
readr	* 2.0.1	2021-08-10	[1]	CRAN	(R 4.0.3)
readxl	1.3.1	2019-03-13	[1]	CRAN	(R 4.0.2)
repr	1.1.3	2021-01-21	[1]	CRAN	(R 4.0.2)
reprex	2.0.1	2021-08-05	[1]	CRAN	(R 4.0.3)
rio	0.5.27	2021-06-21	[1]	CRAN	(R 4.0.3)
rlang	0.4.11	2021-04-30	[1]	CRAN	(R 4.0.3)
rstatix	0.7.0	2021-02-13	[1]	CRAN	(R 4.0.3)
rstudioapi	0.13	2020-11-12	[1]	CRAN	(R 4.0.2)
rvest	1.0.1	2021-07-26	[1]	CRAN	(R 4.0.3)
scales	1.1.1	2020-05-11	[1]	CRAN	(R 4.0.2)
sessioninfo	1.1.1	2018-11-05	[1]	CRAN	(R 4.0.2)
stringi	1.7.4	2021-08-25	[1]	CRAN	(R 4.0.3)
stringr	* 1.4.0	2019-02-10	[1]	CRAN	(R 4.0.2)
svglite	2.0.0	2021-02-20	[1]	CRAN	(R 4.0.3)
systemfonts	1.0.2	2021-05-11	[1]	CRAN	(R 4.0.3)
tibble	* 3.1.4	2021-08-25	[1]	CRAN	(R 4.0.3)
tidyr	* 1.1.3	2021-03-03	[1]	CRAN	(R 4.0.3)
tidyselect	1.1.1	2021-04-30	[1]	CRAN	(R 4.0.3)
tidyverse	* 1.3.1	2021-04-15	[1]	CRAN	(R 4.0.3)
tzdb	0.1.2	2021-07-20	[1]	CRAN	(R 4.0.3)
utf8	1.2.2	2021-07-24	[1]	CRAN	(R 4.0.3)
uuid	0.1-4	2020-02-26	[1]	CRAN	(R 4.0.2)
vctrs	0.3.8	2021-04-29	[1]	CRAN	(R 4.0.3)
withr	2.4.2	2021-04-18	[1]	CRAN	(R 4.0.3)
xml2	1.3.2	2020-04-23	[1]	CRAN	(R 4.0.2)
zip	2.2.0	2021-05-31	[1]	CRAN	(R 4.0.3)

```
[1] /home/jbenja13/R/x86_64-pc-linux-gnu-library/4.0
[2] /usr/lib/R/library
```