Supplementary Text S2: Assessing orthogroup inference in public databases

Fabricio Almeida-Silva [1,2] ***and Yves Van de Peer*** [1,2,3,4]

[1]VIB-UGent Center for Plant Systems Biology, Ghent, Belgium
[2]Department of Plant Biotechnology and Bioinformatics, Ghent University, Ghent, Belgium
[3]College of Horticulture, Academy for Advanced Interdisciplinary Studies, Nanjing Agricultural University, Nanjing, China
[4]Center for Microbial Ecology and Genomics, Department of Biochemistry, Genetics and Microbiology, University of Pretoria, Pretoria, South Africa

14 October 2022

Contents

1 Overview . . . 2
2 Orthogroup assessment . . . 2
2.1 PLAZA Dicots 5.0 . . . 2
2.2 Qiao *et al.*, 2019. Genome Biology . . . 4
2.3 OrthoDB, eggNOG, and HOGENOM . . . 4
3 Comparing homogeneity scores . . . 5
Session info . . . 8
References . . . 11

```
library(cogeqc)
library(here)
library(tidyverse)
library(ggpubr)

set.seed(123) # for reproducibility
source(here("code", "utils.R"))
```

1 Overview

Here, we will use the protein domain-based approach in *cogeqc* to assess gene families from different sources, namely:

- PLAZA Dicots 5.0 (Van Bel et al. 2022)
- OrthoDB (Zdobnov et al. 2021)
- eggNOG (Huerta-Cepas et al. 2019)
- HOGENOM (Penel et al. 2009)
- Qiao et al. (2019)

2 Orthogroup assessment

To make comparison possible, we will *Arabidopsis thaliana* domain annotation as a proxy, as this species is present in all of the aforementioned databases. For that, we will use the function `calculate_H()` from *cogeqc*.

Orthogroups assignments from OrthoDB, eggNOG, InParanoid, PhylomeDB, and HOGENOM will be obtained from UniProt.

2.1 PLAZA Dicots 5.0

Below, we will obtain orthogroups and *A. thaliana*'s domain annotation from PLAZA 5.0, and then we will calculate homogeneity scores for each orthogroup.

```
# Obtain gene families from PLAZA
fams_plaza <- readr::read_tsv(
    paste0(
        "https://ftp.psb.ugent.be/pub/plaza/plaza_public_dicots_05/",
        "GeneFamilies/genefamily_data.HOMFAM.csv.gz"
    ), show_col_types = FALSE, skip = 2
) %>%
    filter(species == "ath") %>%
    as.data.frame()
names(fams_plaza) <- c("Orthogroup", "Species", "Gene")
head(fams_plaza)
##     Orthogroup Species      Gene
## 1 HOM05D000001     ath AT1G02310
## 2 HOM05D000001     ath AT1G03510
## 3 HOM05D000001     ath AT1G03540
## 4 HOM05D000001     ath AT1G04020
```

```
## 5 HOM05D000001     ath AT1G04840
## 6 HOM05D000001     ath AT1G05750

# Obtain domain anotation for A. thaliana
ath_interpro <- readr::read_tsv(
    paste0(
        "https://ftp.psb.ugent.be/pub/plaza/plaza_public_dicots_05/",
        "InterPro/interpro.ath.csv.gz"
    ), show_col_types = FALSE, skip = 8
) %>%
    select(1,3)
names(ath_interpro) <- c("Gene", "Annotation")
head(ath_interpro)
## # A tibble: 6 x 2
##   Gene      Annotation
##   <chr>     <chr>
## 1 AT1G01010 IPR036093
## 2 AT1G01010 IPR003441
## 3 AT1G01010 IPR036093
## 4 AT1G01020 IPR007290
## 5 AT1G01020 IPR007290
## 6 AT1G01030 IPR003340

# Combining everything and calculating homogeneity scores
fam_df_plaza <- merge(fams_plaza, ath_interpro)
head(fam_df_plaza)
##        Gene   Orthogroup Species Annotation
## 1 AT1G01010 HOM05D000010     ath  IPR036093
## 2 AT1G01010 HOM05D000010     ath  IPR003441
## 3 AT1G01010 HOM05D000010     ath  IPR036093
## 4 AT1G01020 HOM05D006082     ath  IPR007290
## 5 AT1G01020 HOM05D006082     ath  IPR007290
## 6 AT1G01030 HOM05D000466     ath  IPR015300

H_summary <- function(ortho_df = NULL) {
    H <- calculate_H(ortho_df)
    mean_H <- round(mean(H$Score), 2)
    median_H <- round(median(H$Score), 2)
    result_list <- list(H = H, mean_score = mean_H, median_score = median_H)
    return(result_list)
}

H_plaza <- H_summary(fam_df_plaza)
head(H_plaza$H)
##     Orthogroup     Score
## 1 HOM05D000001  283.3132
## 2 HOM05D000002  129.9598
## 3 HOM05D000003  889.1268
## 4 HOM05D000004    0.0000
## 5 HOM05D000005 1135.8799
## 6 HOM05D000006 2820.8337
```

2.2 Qiao *et al.*, 2019. Genome Biology

Orthogroups from Qiao et al. (2019) are available in this FigShare repository. The orthogroups information are in the *Orthogroups.csv.zip* file.

```
# Download file and unzip it
download.file(
    url = "https://figshare.com/ndownloader/files/13382270",
    destfile = file.path(tempdir(), "Orthogroups.zip")
)
unzip(
    zipfile = file.path(tempdir(), "Orthogroups.zip"),
    exdir = tempdir()
)

# Get orthogroups
## This file is an old OrthoFinder output without "Orthogroup" in the first row
## Let's add it manually, so it can be parsed with read_orthogroups
og_file <- file.path(tempdir(), "Orthogroups.csv")
l <- readLines(og_file)
l[1] <- paste0("Orthogroup", l[1])
writeLines(l, con = og_file)

## Read and parse file
fam_qiao <- cogeqc::read_orthogroups(og_file) %>%
    mutate(Species = str_replace_all(Species, "\\.pep.*", "")) %>%
    filter(Species == "Ath") %>%
    mutate(Gene = str_replace_all(Gene, "\\.[0-9]$", "")) %>%
    as.data.frame()

# Combining everything and calculating homogeneity scores
fam_df_qiao <- merge(fam_qiao, ath_interpro)
H_qiao <- H_summary(fam_df_qiao)
```

2.3 OrthoDB, eggNOG, and HOGENOM

Orthogroup assignments from these databases will be obtained from UniProt (Consortium 2021).

```
# Get list of proteins - from primary transcripts only
ath_proteome <- Biostrings::readAAStringSet(
    paste0(
        "https://ftp.uniprot.org/pub/databases/uniprot/",
        "current_release/knowledgebase/reference_proteomes/Eukaryota/",
        "UP000006548/UP000006548_3702.fasta.gz"
    )
)
ath_proteins <- names(ath_proteome)
ath_proteins <- sapply(strsplit(ath_proteins, split = "\\|"), `[`, 2)

# Extract phylogenomic information for all genes
```

```
source(here::here("code", "utils.R"))
fams_uniprot <- extract_ogs_uniprot(ath_proteins)

fams_orthodb <- fams_uniprot[, c("Gene", "OrthoDB")] %>% drop_na()
fams_eggnog <- fams_uniprot[, c("Gene", "eggNOG")] %>% drop_na()
fams_hogenom <- fams_uniprot[, c("Gene", "HOGENOM")] %>% drop_na()

#----Calculate homogeneity scores for each database-----------------------------
# OrthoDB
fams_df_orthodb <- merge(fams_orthodb, ath_interpro)
names(fams_df_orthodb)[2] <- "Orthogroup"
H_orthodb <- H_summary(fams_df_orthodb)

# eggNOG
fams_df_eggnog <- merge(fams_eggnog, ath_interpro)
names(fams_df_eggnog)[2] <- "Orthogroup"
H_eggnog <- H_summary(fams_df_eggnog)

# HOGENOM
fams_df_hogenom <- merge(fams_hogenom, ath_interpro)
names(fams_df_hogenom)[2] <- "Orthogroup"
H_hogenom <- H_summary(fams_df_hogenom)
```

3 Comparing homogeneity scores

Finally, let's compare homogeneity scores and visualize their distributions. First, let's combine all data frames of homogeneity scores into a single data frame.

```
H_combined <- bind_rows(
    H_plaza$H %>% mutate(Source = "PLAZA"),
    H_qiao$H %>% mutate(Source = "Qiao et al."),
    H_orthodb$H %>% mutate(Source = "OrthoDB"),
    H_eggnog$H %>% mutate(Source = "eggNOG"),
    H_hogenom$H %>% mutate(Source = "HOGENOM")
)

save(
    H_combined,
    file = here::here("products", "result_files", "H_combined.rda"),
    compress = "xz"
)
```

Now, let's compare the distributions of homogeneity scores for each database to see if there are any differences. For that, we will calculate P-values from a Wilcoxon test with Wicoxon effect sizes (r). The Wilcoxon effect size is calculated as the Z statistic divided by the square root of the sample size.

```
# Scale scores to maximum, so that they range from 0 to 1
H_combined$Score <- H_combined$Score / max(H_combined$Score)
head(H_combined)
```

```
##     Orthogroup      Score Source
## 1 HOM05D000001 0.09785768  PLAZA
## 2 HOM05D000002 0.04488872  PLAZA
## 3 HOM05D000003 0.30710845  PLAZA
## 4 HOM05D000004 0.00000000  PLAZA
## 5 HOM05D000005 0.39233809  PLAZA
## 6 HOM05D000006 0.97432885  PLAZA

# Quick exploration of means and medians
H_combined %>%
    group_by(Source) %>%
    summarise(mean = mean(Score), median = median(Score))
## # A tibble: 5 x 3
##   Source       mean median
##   <chr>       <dbl>  <dbl>
## 1 eggNOG      0.551  0.532
## 2 HOGENOM     0.587  0.594
## 3 OrthoDB     0.563  0.552
## 4 PLAZA       0.594  0.585
## 5 Qiao et al. 0.641  0.634

# Compare homogeneity scores - all vs all
db_wilcox <- compare(H_combined, "Score ~ Source")

db_wilcox[db_wilcox$padj_interpretation != "ns", ]
##     group1      group2   n1   n2 padj_greater padj_less padj_interpretation
## 1   eggNOG     HOGENOM 3092 3257     1.00e+00  9.00e-19                less
## 2   eggNOG     OrthoDB 3092 3201     1.00e+00  7.08e-09                less
## 3   eggNOG       PLAZA 3092 3503     1.00e+00  1.53e-14                less
## 4   eggNOG Qiao et al. 3092 4208     1.00e+00  1.86e-54                less
## 5  HOGENOM     OrthoDB 3257 3201     1.55e-12  1.00e+00             greater
## 6  HOGENOM       PLAZA 3257 3503     1.00e+00  3.00e-03                less
## 7  HOGENOM Qiao et al. 3257 4208     1.00e+00  9.22e-23                less
## 8  OrthoDB       PLAZA 3201 3503     1.00e+00  5.10e-10                less
## 9  OrthoDB Qiao et al. 3201 4208     1.00e+00  1.24e-44                less
## 10   PLAZA Qiao et al. 3503 4208     1.00e+00  7.57e-25                less
##       effsize magnitude
## 1  0.11102956     small
## 2  0.07197679     small
## 3  0.09434683     small
## 4  0.18308505     small
## 5  0.09071787     small
## 6  0.03402610     small
## 7  0.11391762     small
## 8  0.07526911     small
## 9  0.16358811     small
## 10 0.11777755     small
```

We can see that there are diffences in mean. In summary:

1. eggNOG orthogroups have lower scores than every other source

2. HOGENOM orthogroups have higher scores than OrthoDB, but lower than Qiao *et al.* and PLAZA.
3. Orthogroups scores from Qiao *et al* are higher than all other sources.
4. Among the databases (excluding Qiao *et al*), PLAZA orthogroup scores are higher than every other database.

However, the effect sizes are very small, suggesting that significant differences could be due to large sample sizes, as P-values are highly affected by sample sizes.

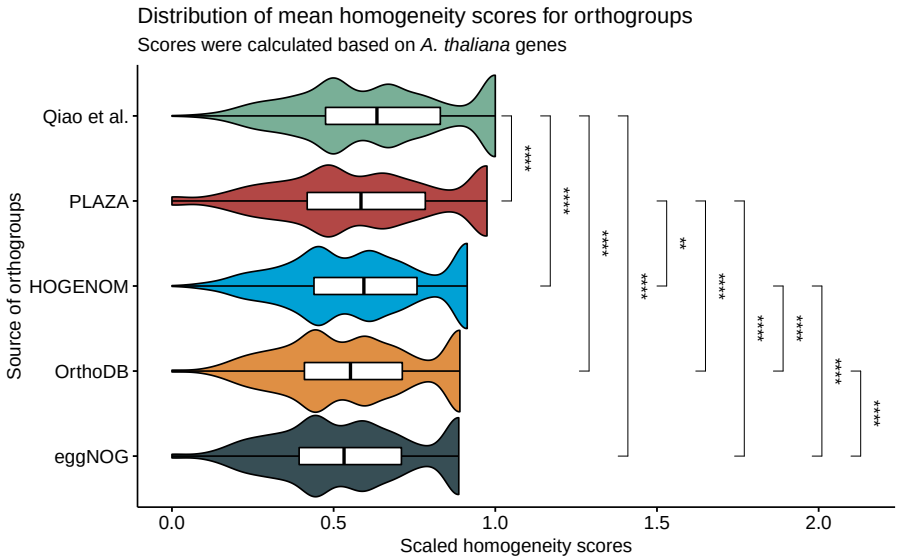
Now, let's visualize the distributions with significant differences highlighted.

```
# Comparisons to be made
comps <- list(
    c("Qiao et al.", "PLAZA"),
    c("Qiao et al.", "HOGENOM"),
    c("Qiao et al.", "OrthoDB"),
    c("Qiao et al.", "eggNOG"),
    c("PLAZA", "HOGENOM"),
    c("PLAZA", "OrthoDB"),
    c("PLAZA", "eggNOG"),
    c("HOGENOM", "OrthoDB"),
    c("HOGENOM", "eggNOG"),
    c("OrthoDB", "eggNOG")
)

# Change order of levels according to comparison results
H_combined$Source <- factor(
    H_combined$Source, levels = rev(c(
        "Qiao et al.", "PLAZA", "HOGENOM", "OrthoDB", "eggNOG"
    ))
)

# Visualize distributions with significant differences highlighted
distros <- ggviolin(
    H_combined, y = "Score", x = "Source",
    orientation = "horiz", trim = TRUE, add = "boxplot",
    fill = "Source", add.params = list(fill = "white"), palette = "jama"
) +
    ggpubr::stat_compare_means(
        comparisons = comps,
        label = "p.signif",
        method = "wilcox.test"
    ) +
    theme(legend.position = "none") +
    labs(y = "Scaled homogeneity scores", x = "Source of orthogroups",
         title = "Distribution of mean homogeneity scores for orthogroups",
         subtitle = "Scores were calculated based on *A. thaliana* genes") +
    theme(plot.subtitle = ggtext::element_markdown())

distros
```



To conclude, despite some significant differences, all databases perform equally well in their orthogroup definition. The observed differences in means could be due to large sample sizes, as indicated by very low effect sizes, and to the different species composition of the database.

Session info

This document was created under the following conditions:

```
sessioninfo::session_info()
## - Session info -------------------------------------------------------------
##  setting  value
##  version  R version 4.2.1 (2022-06-23)
##  os       Ubuntu 20.04.4 LTS
##  system   x86_64, linux-gnu
##  ui       X11
##  language (EN)
##  collate  en_US.UTF-8
##  ctype    en_US.UTF-8
##  tz       Europe/Brussels
##  date     2022-10-14
##  pandoc   2.18 @ /usr/lib/rstudio/bin/quarto/bin/tools/ (via rmarkdown)
##
## - Packages -----------------------------------------------------------------
##  package          * version  date (UTC) lib source
##  abind              1.4-5    2016-07-21 [1] CRAN (R 4.2.0)
##  ape                5.6-2    2022-03-02 [1] CRAN (R 4.2.0)
##  aplot              0.1.8    2022-10-09 [1] CRAN (R 4.2.1)
##  assertthat         0.2.1    2019-03-21 [1] CRAN (R 4.2.0)
##  backports          1.4.1    2021-12-13 [1] CRAN (R 4.2.0)
##  BiocGenerics       0.42.0   2022-04-26 [1] Bioconductor
##  BiocManager        1.30.18  2022-05-18 [1] CRAN (R 4.2.0)
##  BiocStyle        * 2.25.0   2022-06-15 [1] Github (Bioconductor/BiocStyle@7150c28)
```

```
##  Biostrings         2.64.1   2022-08-18 [1] Bioconductor
##  bit                4.0.4    2020-08-04 [1] CRAN (R 4.2.0)
##  bit64              4.0.5    2020-08-30 [1] CRAN (R 4.2.0)
##  bitops             1.0-7    2021-04-24 [1] CRAN (R 4.2.0)
##  bookdown           0.29     2022-09-12 [1] CRAN (R 4.2.1)
##  broom              1.0.1    2022-08-29 [1] CRAN (R 4.2.1)
##  car                3.1-0    2022-06-15 [1] CRAN (R 4.2.0)
##  carData            3.0-5    2022-01-06 [1] CRAN (R 4.2.0)
##  cellranger         1.1.0    2016-07-27 [1] CRAN (R 4.2.0)
##  cli                3.4.1    2022-09-23 [1] CRAN (R 4.2.1)
##  codetools          0.2-18   2020-11-04 [1] CRAN (R 4.2.0)
##  cogeqc           * 1.1.7    2022-10-13 [1] Github (almeidasilvaf/cogeqc@691c44b)
##  coin               1.4-2    2021-10-08 [1] CRAN (R 4.2.1)
##  colorspace         2.0-3    2022-02-21 [1] CRAN (R 4.2.0)
##  crayon             1.5.2    2022-09-29 [1] CRAN (R 4.2.1)
##  curl               4.3.3    2022-10-06 [1] CRAN (R 4.2.1)
##  DBI                1.1.3    2022-06-18 [1] CRAN (R 4.2.0)
##  dbplyr             2.2.1    2022-06-27 [1] CRAN (R 4.2.1)
##  digest             0.6.29   2021-12-01 [1] CRAN (R 4.2.0)
##  dplyr            * 1.0.10   2022-09-01 [1] CRAN (R 4.2.1)
##  ellipsis           0.3.2    2021-04-29 [1] CRAN (R 4.2.0)
##  evaluate           0.17     2022-10-07 [1] CRAN (R 4.2.1)
##  fansi              1.0.3    2022-03-24 [1] CRAN (R 4.2.0)
##  farver             2.1.1    2022-07-06 [1] CRAN (R 4.2.1)
##  fastmap            1.1.0    2021-01-25 [1] CRAN (R 4.2.0)
##  forcats          * 0.5.2    2022-08-19 [1] CRAN (R 4.2.1)
##  fs                 1.5.2    2021-12-08 [1] CRAN (R 4.2.0)
##  gargle             1.2.1    2022-09-08 [1] CRAN (R 4.2.1)
##  generics           0.1.3    2022-07-05 [1] CRAN (R 4.2.1)
##  GenomeInfoDb       1.32.4   2022-09-06 [1] Bioconductor
##  GenomeInfoDbData   1.2.8    2022-05-06 [1] Bioconductor
##  ggfun              0.0.7    2022-08-31 [1] CRAN (R 4.2.1)
##  ggplot2          * 3.3.6    2022-05-03 [1] CRAN (R 4.2.0)
##  ggplotify          0.1.0    2021-09-02 [1] CRAN (R 4.2.0)
##  ggpubr           * 0.4.0    2020-06-27 [1] CRAN (R 4.2.0)
##  ggsci              2.9      2018-05-14 [1] CRAN (R 4.2.0)
##  ggsignif           0.6.4    2022-10-13 [1] CRAN (R 4.2.1)
##  ggtext             0.1.2    2022-09-16 [1] CRAN (R 4.2.1)
##  ggtree             3.4.4    2022-09-27 [1] Bioconductor
##  glue               1.6.2    2022-02-24 [1] CRAN (R 4.2.0)
##  googledrive        2.0.0    2021-07-08 [1] CRAN (R 4.2.0)
##  googlesheets4      1.0.1    2022-08-13 [1] CRAN (R 4.2.1)
##  gridGraphics       0.5-1    2020-12-13 [1] CRAN (R 4.2.0)
##  gridtext           0.1.5    2022-09-16 [1] CRAN (R 4.2.1)
##  gtable             0.3.1    2022-09-01 [1] CRAN (R 4.2.1)
##  haven              2.5.1    2022-08-22 [1] CRAN (R 4.2.1)
##  here             * 1.0.1    2020-12-13 [1] CRAN (R 4.2.0)
##  hms                1.1.2    2022-08-19 [1] CRAN (R 4.2.1)
##  htmltools          0.5.3    2022-07-18 [1] CRAN (R 4.2.1)
##  httr               1.4.4    2022-08-17 [1] CRAN (R 4.2.1)
##  igraph             1.3.5    2022-09-22 [1] CRAN (R 4.2.1)
```

```
##  IRanges           2.30.1   2022-08-18 [1] Bioconductor
##  jsonlite          1.8.2    2022-10-02 [1] CRAN (R 4.2.1)
##  knitr             1.40     2022-08-24 [1] CRAN (R 4.2.1)
##  labeling          0.4.2    2020-10-20 [1] CRAN (R 4.2.0)
##  lattice           0.20-45  2021-09-22 [1] CRAN (R 4.2.0)
##  lazyeval          0.2.2    2019-03-15 [1] CRAN (R 4.2.0)
##  libcoin           1.0-9    2021-09-27 [1] CRAN (R 4.2.1)
##  lifecycle         1.0.3    2022-10-07 [1] CRAN (R 4.2.1)
##  lubridate         1.8.0    2021-10-07 [1] CRAN (R 4.2.0)
##  magrittr          2.0.3    2022-03-30 [1] CRAN (R 4.2.0)
##  markdown          1.1      2019-08-07 [1] CRAN (R 4.2.0)
##  MASS              7.3-58.1 2022-08-03 [1] CRAN (R 4.2.1)
##  Matrix            1.5-1    2022-09-13 [1] CRAN (R 4.2.1)
##  matrixStats       0.62.0   2022-04-19 [1] CRAN (R 4.2.0)
##  modelr            0.1.9    2022-08-19 [1] CRAN (R 4.2.1)
##  modeltools        0.2-23   2020-03-05 [1] CRAN (R 4.2.1)
##  multcomp          1.4-20   2022-08-07 [1] CRAN (R 4.2.1)
##  munsell           0.5.0    2018-06-12 [1] CRAN (R 4.2.0)
##  mvtnorm           1.1-3    2021-10-08 [1] CRAN (R 4.2.0)
##  nlme              3.1-160  2022-10-10 [1] CRAN (R 4.2.1)
##  patchwork         1.1.2    2022-08-19 [1] CRAN (R 4.2.1)
##  pillar            1.8.1    2022-08-19 [1] CRAN (R 4.2.1)
##  pkgconfig         2.0.3    2019-09-22 [1] CRAN (R 4.2.0)
##  plyr              1.8.7    2022-03-24 [1] CRAN (R 4.2.0)
##  purrr           * 0.3.5    2022-10-06 [1] CRAN (R 4.2.1)
##  R6                2.5.1    2021-08-19 [1] CRAN (R 4.2.0)
##  Rcpp              1.0.9    2022-07-08 [1] CRAN (R 4.2.1)
##  RCurl             1.98-1.9 2022-10-03 [1] CRAN (R 4.2.1)
##  readr           * 2.1.3    2022-10-01 [1] CRAN (R 4.2.1)
##  readxl            1.4.1    2022-08-17 [1] CRAN (R 4.2.1)
##  reprex            2.0.2    2022-08-17 [1] CRAN (R 4.2.1)
##  reshape2          1.4.4    2020-04-09 [1] CRAN (R 4.2.0)
##  rlang             1.0.6    2022-09-24 [1] CRAN (R 4.2.1)
##  rmarkdown         2.17     2022-10-07 [1] CRAN (R 4.2.1)
##  rprojroot         2.0.3    2022-04-02 [1] CRAN (R 4.2.0)
##  rstatix           0.7.0    2021-02-13 [1] CRAN (R 4.2.1)
##  rstudioapi        0.14     2022-08-22 [1] CRAN (R 4.2.1)
##  rvest             1.0.3    2022-08-19 [1] CRAN (R 4.2.1)
##  S4Vectors         0.34.0   2022-04-26 [1] Bioconductor
##  sandwich          3.0-2    2022-06-15 [1] CRAN (R 4.2.1)
##  scales            1.2.1    2022-08-20 [1] CRAN (R 4.2.1)
##  sessioninfo       1.2.2    2021-12-06 [1] CRAN (R 4.2.0)
##  stringi           1.7.8    2022-07-11 [1] CRAN (R 4.2.1)
##  stringr         * 1.4.1    2022-08-20 [1] CRAN (R 4.2.1)
##  survival          3.4-0    2022-08-09 [1] CRAN (R 4.2.1)
##  TH.data           1.1-1    2022-04-26 [1] CRAN (R 4.2.1)
##  tibble          * 3.1.8    2022-07-22 [1] CRAN (R 4.2.1)
##  tidyr           * 1.2.1    2022-09-08 [1] CRAN (R 4.2.1)
##  tidyselect        1.2.0    2022-10-10 [1] CRAN (R 4.2.1)
##  tidytree          0.4.1    2022-09-26 [1] CRAN (R 4.2.1)
##  tidyverse       * 1.3.2    2022-07-18 [1] CRAN (R 4.2.1)
```

```
##  treeio             1.20.2   2022-08-14 [1] Bioconductor
##  tzdb               0.3.0    2022-03-28 [1] CRAN (R 4.2.0)
##  utf8               1.2.2    2021-07-24 [1] CRAN (R 4.2.0)
##  vctrs              0.4.2    2022-09-29 [1] CRAN (R 4.2.1)
##  vroom              1.6.0    2022-09-30 [1] CRAN (R 4.2.1)
##  withr              2.5.0    2022-03-03 [1] CRAN (R 4.2.0)
##  xfun               0.33     2022-09-12 [1] CRAN (R 4.2.1)
##  xml2               1.3.3    2021-11-30 [1] CRAN (R 4.2.0)
##  XVector            0.36.0   2022-04-26 [1] Bioconductor
##  yaml               2.3.5    2022-02-21 [1] CRAN (R 4.2.0)
##  yulab.utils        0.0.5    2022-06-30 [1] CRAN (R 4.2.1)
##  zlibbioc           1.42.0   2022-04-26 [1] Bioconductor
##  zoo                1.8-11   2022-09-17 [1] CRAN (R 4.2.1)
##
##  [1] /home/faalm/R/x86_64-pc-linux-gnu-library/4.2
##  [2] /usr/local/lib/R/site-library
##  [3] /usr/lib/R/site-library
##  [4] /usr/lib/R/library
##
## ------------------------------------------------------------------------------
```

References

Consortium, The UniProt. 2021. "UniProt: The Universal Protein Knowledgebase in 2021." *Nucleic Acids Research* 49 (D1): D480–89.

Huerta-Cepas, Jaime, Damian Szklarczyk, Davide Heller, Ana Hernández-Plaza, Sofia K Forslund, Helen Cook, Daniel R Mende, et al. 2019. "eggNOG 5.0: A Hierarchical, Functionally and Phylogenetically Annotated Orthology Resource Based on 5090 Organisms and 2502 Viruses." *Nucleic Acids Research* 47 (D1): D309–14.

Penel, Simon, Anne-Muriel Arigon, Jean-François Dufayard, Anne-Sophie Sertier, Vincent Daubin, Laurent Duret, Manolo Gouy, and Guy Perrière. 2009. "Databases of Homologous Gene Families for Comparative Genomics." In *BMC Bioinformatics*, 10:1–13. 6. BioMed Central.

Qiao, Xin, Qionghou Li, Hao Yin, Kaijie Qi, Leiting Li, Runze Wang, Shaoling Zhang, and Andrew H Paterson. 2019. "Gene Duplication and Evolution in Recurring Polyploidization–Diploidization Cycles in Plants." *Genome Biology* 20 (1): 1–23.

Van Bel, Michiel, Francesca Silvestri, Eric M Weitz, Lukasz Kreft, Alexander Botzki, Frederik Coppens, and Klaas Vandepoele. 2022. "PLAZA 5.0: Extending the Scope and Power of Comparative and Functional Genomics in Plants." *Nucleic Acids Research* 50 (D1): D1468–74.

Zdobnov, Evgeny M, Dmitry Kuznetsov, Fredrik Tegenfeldt, Mosè Manni, Matthew Berkeley, and Evgenia V Kriventseva. 2021. "OrthoDB in 2020: Evolutionary and Functional Annotations of Orthologs." *Nucleic Acids Research* 49 (D1): D389–93.