# Package 'orthogene'

March 14, 2023

```
Type Package
Title Interspecies gene mapping
Version 1.5.1
Description `orthogene` is an R package for easy mapping of orthologous genes
      across hundreds of species. It pulls up-to-date gene ortholog mappings
      across **700+ organisms**.
      It also provides various utility functions to aggregate/expand
      common objects (e.g. data.frames, gene expression matrices, lists)
      using **1:1**, **many:1**, **1:many** or **many:many** gene mappings,
      both within- and between-species.
URL https://github.com/neurogenomics/orthogene
BugReports https://github.com/neurogenomics/orthogene/issues
License GPL-3
Depends R (>= 4.1)
VignetteBuilder knitr
biocViews Genetics, ComparativeGenomics, Preprocessing,
      Phylogenetics, Transcriptomics, GeneExpression
Imports dplyr,
      methods,
      stats,
      utils,
      Matrix,
      jsonlite,
      homologene,
      gprofiler2,
      babelgene,
      data.table,
      parallel,
      ggplot2,
      ggpubr,
      patchwork,
      DelayedArray,
      grr,
      repmis,
      ggtree,
      tools
```

2 R topics documented:

Suggests re	motes,
knitr,	
BiocS	tyle,
covr,	
marko	
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here,	
	at $(>= 3.0.0)$ ,
piggy	
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magic	k,
desc,	
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orthogene-package

orthogene: Interspecies gene mapping

#### **Description**

**orthogene** is an R package for easy mapping of orthologous genes across hundreds of species.

#### **Details**

It pulls up-to-date interspecies gene ortholog mappings across 700+ organisms. It also provides various utility functions to map common objects (e.g. data.frames, gene expression matrices, lists) onto 1:1 gene orthologs from any other species.

# Author(s)

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#### **Source**

- GitHub: Source code and Issues submission.
- Author Site: orthogene was created by Brian M. Schilder.

#### See Also

Useful links:

- https://github.com/neurogenomics/orthogene
- Report bugs at https://github.com/neurogenomics/orthogene/issues

aggregate\_mapped\_genes

Aggregate/expand a gene matrix by gene mappings

# Description

Aggregate/expand a gene matrix (gene\_df) using a gene mapping data.frame (gene\_map). Importantly, mappings can be performed across a variety of scenarios that can occur during within-species and between-species gene mapping:

1 gene : 1 genemany genes : 1 gene

• 1 gene : many genes

• many genes : many genes

For more details on how aggregation/expansion is performed, please see: many2many\_rows.

#### Usage

```
aggregate_mapped_genes(
  gene_df,
 gene_map = NULL,
  input_col = "input_gene",
  output_col = "ortholog_gene",
  input_species = "human",
  output_species = input_species,
 method = c("gprofiler", "homologene", "babelgene"),
  agg_fun = "sum",
  agg_method = c("monocle3", "stats"),
  aggregate_orthologs = TRUE,
  transpose = FALSE,
 mthreshold = 1,
  target = "ENSG",
  numeric_ns = ""
  as_integers = FALSE,
  as\_sparse = TRUE,
  as_DelayedArray = FALSE,
 dropNA = TRUE,
  sort_rows = FALSE,
  verbose = TRUE
```

#### **Arguments**

gene\_df

Input matrix where row names are genes.

gene\_map

A data.frame that maps the current gene names to new gene names. This function's behaviour will adapt to different situations as follows:

- gene\_map=<data.frame>: When a data.frame containing the gene key:value columns (specified by input\_col and output\_col, respectively) is provided, this will be used to perform aggregation/expansion.
- gene\_map=NULL and input\_species!=output\_species: A gene\_map is automatically generated by map\_orthologs to perform interspecies gene aggregation/expansion.
- gene\_map=NULL and input\_species==output\_species: A gene\_map is automatically generated by map genes to perform withinspecies gene gene symbol standardization and aggregation/expansion.

input\_col

Column name within gene\_map with gene names matching the row names of X.

output\_col

Column name within gene\_map with gene names that you wish you map the row names of X onto.

input\_species

Name of the input species (e.g., "mouse", "fly"). Use map\_species to return a full list of available species.

output\_species Name of the output species (e.g. "human", "chicken"). Use map\_species to return a full list of available species.

method

R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.

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• "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

agg\_fun Aggregation function.
agg\_method Aggregation method.

aggregate\_orthologs

[Optional] After performing an initial round of many:many aggregation/expansion with many2many\_rows, ensure each orthologous gene only appears in one row

by using the aggregate\_rows function (default: TRUE).

transpose gene\_df before mapping genes.

mthreshold maximum number of results per initial alias to show. Shows all by default.

target target namespace.

numeric\_ns namespace to use for fully numeric IDs (list of available namespaces).

as\_integers Force all values in the matrix to become integers, by applying floor (default:

FALSE).

as\_sparse Convert aggregated matrix to sparse matrix.

as\_DelayedArray

Convert aggregated matrix to DelayedArray.

dropNA Drop genes assigned to NA in groupings.
sort\_rows Sort gene\_df rows alphanumerically.

verbose Print messages.

#### Value

Aggregated matrix

# Examples

all\_genes Get all genes

# Description

Return all known genes from a given species.

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#### Usage

```
all_genes(
   species,
   method = c("gprofiler", "homologene", "babelgene"),
   ensure_filter_nas = FALSE,
   run_map_species = TRUE,
   verbose = TRUE,
   ...
)
```

#### **Arguments**

species

Species to get all genes for. Will first be standardised with map\_species.

method

R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

ensure\_filter\_nas

Perform an extra check to remove genes that are NAs of any kind.

run\_map\_species

Standardise species names with map\_species first (Default: TRUE).

verbose

Print messages.

.. Additional arguments to be passed to gorth or homologene.

*NOTE*: To return only the most "popular" interspecies ortholog mappings, supply mthreshold=1 here AND set method="gprofiler" above. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.

For more details, please see here.

## Details

References homologeneData or gconvert.

#### Value

Table with all gene symbols from the given species.

```
genome_mouse <- all_genes(species = "mouse")
genome_human <- all_genes(species = "human")</pre>
```

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convert\_orthologs

Map genes from one species to another

## **Description**

Currently supports ortholog mapping between any pair of 700+ species. Use map\_species to return a full list of available organisms.

#### Usage

```
convert_orthologs(
  gene_df,
  gene_input = "rownames",
  gene_output = "rownames"
  standardise_genes = FALSE,
  input_species,
  output_species = "human",
  method = c("gprofiler", "homologene", "babelgene"),
  drop_nonorths = TRUE,
  non121_strategy = "drop_both_species",
  agg_fun = NULL,
  mthreshold = Inf,
  as_sparse = FALSE,
  as_DelayedArray = FALSE,
  sort_rows = FALSE,
  verbose = TRUE,
)
```

# Arguments

gene\_df

Data object containing the genes (see gene\_input for options on how the genes can be stored within the object).

Can be one of the following formats:

• matrix:

A sparse or dense matrix.

• data.frame:

A data.frame, data.table.ortibble.

• codelist:

A list or character vector.

Genes, transcripts, proteins, SNPs, or genomic ranges can be provided in any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and will be automatically converted to gene symbols unless specified otherwise with the . . . arguments. *Note*: If you set method="homologene", you must either supply genes in gene symbol format (e.g. "Sox2") OR set standardise\_genes=TRUE.

gene\_input

Which aspect of gene\_df to get gene names from:

• "rownames":

From row names of data.frame/matrix.

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• "colnames":

From column names of data.frame/matrix.

• <column name>:

From a column in gene\_df, e.g. "gene\_names".

gene\_output

How to return genes. Options include:

• "rownames":

As row names of gene\_df.

• "colnames":

As column names of gene\_df.

• "columns":

As new columns "input\_gene", "ortholog\_gene" (and "input\_gene\_standard" if standardise\_genes=TRUE) in gene\_df.

• "dict":

As a dictionary (named list) where the names are input\_gene and the values are ortholog\_gene.

"dict\_rev":

As a reversed dictionary (named list) where the names are ortholog\_gene and the values are input gene.

standardise\_genes

If TRUE AND gene\_output="columns", a new column "input\_gene\_standard" will be added to gene\_df containing standardised HGNC symbols identified by gorth.

input\_species

Name of the input species (e.g., "mouse", "fly"). Use map\_species to return a full list of available species.

output\_species Name of the output species (e.g. "human", "chicken"). Use map\_species to return a full list of available species.

method

R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

drop\_nonorths non121\_strategy

Drop genes that don't have an ortholog in the output\_species.

How to handle genes that don't have 1:1 mappings between input\_species:output\_species.

• "drop\_both\_species" or "dbs" or 1: Drop genes that have duplicate mappings in either the input\_species or

(DEFAULT).

output\_species

Options include:

• "drop\_input\_species" or "dis" or 2: Only drop genes that have duplicate mappings in the input\_species.

- "drop\_output\_species" or "dos" or 3: Only drop genes that have duplicate mappings in the output\_species.
- "keep\_both\_species" or "kbs" or 4: Keep all genes regardless of whether they have duplicate mappings in either species.

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- "keep\_popular" or "kp" or 5: Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.
- "sum", "mean", "median", "min" or "max":

  When gene\_df is a matrix and gene\_output="rownames", these options
  will aggregate many-to-one gene mappings (input\_species-to-output\_species)
  after dropping any duplicate genes in the output\_species.

agg\_fun

Aggregation function passed to aggregate\_mapped\_genes. Set to NULL to skip aggregation step (default).

mthreshold

Maximum number of ortholog names per gene to show. Passed to gorth. Only used when method="gprofiler" (*DEFAULT*: Inf).

as\_sparse

Convert gene\_df to a sparse matrix. Only works if gene\_df is one of the following classes:

- matrix
- Matrix
- data.frame
- data.table
- tibble

If gene\_df is a sparse matrix to begin with, it will be returned as a sparse matrix (so long as gene\_output= "rownames" or "colnames").

as\_DelayedArray

Convert aggregated matrix to DelayedArray.

sort\_rows

Sort gene\_df rows alphanumerically.

verbose

Print messages.

Additional arguments to be passed to gorth or homologene.

*NOTE*: To return only the most "popular" interspecies ortholog mappings, supply mthreshold=1 here AND set method="gprofiler" above. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.

For more details, please see here.

# Value

```
gene_df with orthologs converted to the output_species.

Instead returned as a dictionary (named list) if gene_output="dict" or "dict_rev".
```

```
data("exp_mouse")
gene_df <- convert_orthologs(
    gene_df = exp_mouse,
    input_species = "mouse"
)</pre>
```

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create\_background

Create gene background

## **Description**

Create a gene background as the union/intersect of all orthologs between input species (species1 and species2), and the output\_species. This can be useful when generating random lists of background genes to test against in analyses with data from multiple species (e.g. enrichment of mouse cell-type markers gene sets in human GWAS-derived gene sets).

#### Usage

```
create_background(
  species1,
  species2,
  output_species = "human",
  as_output_species = TRUE,
  use_intersect = TRUE,
  bg = NULL,
  gene_map = NULL,
  method = "homologene",
  non121_strategy = "drop_both_species",
  verbose = TRUE
)
```

# **Arguments**

species1 First species.

species2 Second species.

output\_species Species to convert all genes from species1 and species2 to first. Default="human",

but can be to either any species supported by **orthogene**, including species1 or

species2.

as\_output\_species

Return background gene list as output\_species orthologs, instead of the gene

names of the original input species.

use\_intersect When species1 and species2 are both different from output\_species, this

argument will determine whether to use the intersect (TRUE) or union (FALSE) of

all genes from species1 and species2.

bg User supplied background list that will be returned to the user after removing

duplicate genes.

method R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

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non121\_strategy

How to handle genes that don't have 1:1 mappings between input\_species:output\_species. Options include:

- "drop\_both\_species" or "dbs" or 1:
   Drop genes that have duplicate mappings in either the input\_species or output\_species
   (DEFAULT).
- "drop\_input\_species" or "dis" or 2:
  Only drop genes that have duplicate mappings in the input\_species.
- "drop\_output\_species" or "dos" or 3:
  Only drop genes that have duplicate mappings in the output\_species.
- "keep\_both\_species" or "kbs" or 4:
  Keep all genes regardless of whether they have duplicate mappings in either species.
- "keep\_popular" or "kp" or 5:
  Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.
- "sum", "mean", "median", "min" or "max":

  When gene\_df is a matrix and gene\_output="rownames", these options
  will aggregate many-to-one gene mappings (input\_species-to-output\_species)
  after dropping any duplicate genes in the output\_species.

verbose

Print messages.

## Value

Background gene list.

# **Examples**

exp\_mouse

Gene expression data: mouse

#### **Description**

 $Mean\ pseudobulk\ single-cell\ RNA-seq\ gene\ expression\ matrix.$ 

Data originally comes from Zeisel et al., 2018 (Cell).

## Usage

```
data("exp_mouse")
```

#### **Format**

sparse matrix

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#### **Source**

Publication ctd <- ewceData::ctd() exp\_mouse <- as(ctd[[1]]\$mean\_exp, "sparseMatrix")
usethis::use\_data(exp\_mouse, overwrite = TRUE)</pre>

exp\_mouse\_enst

Transcript expression data: mouse

## **Description**

Mean pseudobulk single-cell RNA-seq Transcript expression matrix. Data originally comes from Zeisel et al., 2018 (Cell).

# Usage

```
data("exp_mouse_enst")
```

#### **Format**

sparse matrix

#### **Source**

Publication data("exp\_mouse") mapped\_genes <- map\_genes(genes = rownames(exp\_mouse)[seq(1,100)],
target = "ENST", species = "mouse", drop\_na = FALSE) exp\_mouse\_enst <- exp\_mouse[mapped\_genes\$input,]
rownames(exp\_mouse\_enst) <- mapped\_genes\$target all\_nas <- orthogene:::find\_all\_nas(rownames(exp\_m
exp\_mouse\_enst <- exp\_mouse\_enst[!all\_nas,] exp\_mouse\_enst <- phenomix::add\_noise(exp\_mouse\_enst)
usethis::use\_data(exp\_mouse\_enst, overwrite = TRUE)</pre>

gprofiler\_namespace

gconvert namespaces

## Description

Available namespaces used by link[gprofiler2]gconvert.

#### **Format**

data.frame

## Source

# gProfiler site

```
#### Manually-prepared CSV #### path <- "inst/extdata/gprofiler_namespace.csv.gz" gprofiler_namespa
<- data.table::fread(path)</pre>
```

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gprofiler\_orgs

Reference organisms

#### **Description**

Organism for which gene references are available via gProfiler API. Used as a backup if API is not available.

#### **Format**

data.frame

#### Source

#### gProfiler site

# NOTE!: Must run usethis::use\_data for all internal data at once. # otherwise, the prior
internal data will be overwritten. #### Internal data 1: gprofiler\_namespace #### ####
Manually-prepared CSV #### path <- "inst/extdata/gprofiler\_namespace.csv.gz" gprofiler\_namespace
<- data.table::fread(path) #### Internal data 2: gprofiler\_orgs gprofiler\_orgs <- orthogene:::get\_or
#### Save #### usethis::use\_data(gprofiler\_orgs,gprofiler\_namespace, overwrite = TRUE,
internal=TRUE)</pre>

infer\_species

Infer species from gene names

#### **Description**

Infers which species the genes within gene\_df is from. Iteratively test the percentage of gene\_df genes that match with the genes from each test\_species.

# Usage

```
infer_species(
  gene_df,
  gene_input = "rownames",
  test_species = c("human", "monkey", "rat", "mouse", "zebrafish", "fly"),
  method = c("homologene", "gprofiler", "babelgene"),
  make_plot = TRUE,
  show_plot = TRUE,
  verbose = TRUE
)
```

## **Arguments**

gene\_df

Data object containing the genes (see gene\_input for options on how the genes can be stored within the object).

Can be one of the following formats:

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• matrix:

A sparse or dense matrix.

• data.frame:

A data.frame, data.table. or tibble.

• codelist:

A list or character vector.

Genes, transcripts, proteins, SNPs, or genomic ranges can be provided in any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and will be automatically converted to gene symbols unless specified otherwise with the . . . arguments. *Note*: If you set method="homologene", you must either supply genes in gene symbol format (e.g. "Sox2") OR set standardise\_genes=TRUE.

gene\_input

Which aspect of gene\_df to get gene names from:

• "rownames":

From row names of data.frame/matrix.

• "colnames":

From column names of data.frame/matrix.

• <column name>:

From a column in gene\_df, e.g. "gene\_names".

test\_species

Which species to test for matches with. If set to NULL, will default to a list of humans and 5 common model organisms. If test\_species is set to one of the following options, it will automatically pull all species from that respective package and test against each of them:

• "homologene": 20+ species (default)

• "gprofiler" : 700+ species

• "babelgene": 19 species

method

R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

make\_plot Make a plot of the results.

show\_plot Print the plot of the results.

verbose Print messages.

#### Value

An ordered dataframe of test\_species from best to worst matches.

```
data("exp_mouse")
matches <- orthogene::infer_species(gene_df = exp_mouse[1:200,])</pre>
```

map\_genes 15

map_genes	Map genes
-----------	-----------

# Description

Input a list of genes, transcripts, proteins, SNPs, or genomic ranges in any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and return a table with standardised gene symbols (the "names" column).

#### Usage

```
map_genes(
   genes,
   species = "hsapiens",
   target = "ENSG",
   mthreshold = Inf,
   drop_na = FALSE,
   numeric_ns = "",
   run_map_species = TRUE,
   verbose = TRUE
```

## **Arguments**

genes Gene list. Species to map against. species target target namespace. mthreshold maximum number of results per initial alias to show. Shows all by default. Drop all genes without mappings. Sets gprofiler2::gconvert(filter\_na=) drop\_na as well an additional round of more comprehensive NA filtering by orthogene. namespace to use for fully numeric IDs (list of available namespaces). numeric\_ns run\_map\_species Standardise species names with map\_species first (Default: TRUE). verbose Print messages.

# Details

Uses gconvert. The exact contents of the output table will depend on target parameter. See ?gprofiler2::gconvert for more details.

#### Value

Table with standardised genes.

```
genes <- c(
    "Klf4", "Sox2", "TSPAN12", "NM_173007", "Q8BKT6",
    "ENSMUSG00000012396", "ENSMUSG00000074637"
)
mapped_genes <- map_genes(</pre>
```

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```
genes = genes,
    species = "mouse"
)
```

map\_orthologs

Map orthologs

#### **Description**

Map orthologs from one species to another.

## Usage

```
map_orthologs(
  genes,
  standardise_genes = FALSE,
  input_species,
  output_species = "human".
  method = c("gprofiler", "homologene", "babelgene"),
  mthreshold = Inf,
  verbose = TRUE,
)
```

#### **Arguments**

genes

can be a mixture of any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and will be automatically converted to standardised HGNC symbol format.

standardise\_genes

If TRUE AND gene\_output="columns", a new column "input\_gene\_standard" will be added to gene\_df containing standardised HGNC symbols identified by gorth.

input\_species

Name of the input species (e.g., "mouse", "fly"). Use map\_species to return a full list of available species.

output\_species Name of the output species (e.g. "human", "chicken"). Use map\_species to return a full list of available species.

method

R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

mthreshold

Maximum number of ortholog names per gene to show. Passed to gorth. Only used when method="gprofiler" (DEFAULT: Inf).

verbose

Print messages.

. . .

Additional arguments to be passed to gorth or homologene.

NOTE: To return only the most "popular" interspecies ortholog mappings, supply mthreshold=1 here AND set method="gprofiler" above. This procedure tends to yield a greater number of returned genes but at the cost of many of them map\_species 17

not being true biological 1:1 orthologs.

For more details, please see here.

#### **Details**

map\_orthologs() is a core function within convert\_orthologs(), but does not have many of the extra checks, such as non121\_strategy) and drop\_nonorths.

#### Value

Ortholog map data.frame with at least the columns "input\_gene" and "ortholog\_gene".

## **Examples**

```
data("exp_mouse")
gene_map <- map_orthologs(
    genes = rownames(exp_mouse),
    input_species = "mouse"
)</pre>
```

map\_species

Standardise species names

#### **Description**

Search gprofiler database for species that match the input text string. Then translate to a standardised species ID.

## Usage

```
map_species(
  species = NULL,
  search_cols = c("display_name", "id", "scientific_name", "taxonomy_id"),
  output_format = c("scientific_name", "id", "display_name", "taxonomy_id", "version"),
  method = c("homologene", "gprofiler", "babelgene"),
  use_local = TRUE,
  verbose = TRUE
)
```

#### **Arguments**

species

Species query (e.g. "human", "homo sapiens", "hapiens", or 9606). If given a

list, will iterate queries for each item. Set to NULL to return all species.

search\_cols

Which columns to search for species substring in metadata API.

output\_format

Which column to return.

method

R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

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use\_local If TRUE default, map species uses a locally stored version of the species metadata table instead of pulling directly from the gprofiler API. Local version may not be fully up to date, but should suffice for most use cases. verbose

Print messages.

#### Value

```
Species ID of type output_format
```

#### **Examples**

```
ids <- map_species(species = c(</pre>
    "human", 9606, "mus musculus",
    "fly", "C elegans"
))
```

plot\_orthotree

Create a phylogenetic tree of shared orthologs

# Description

Automatically creates a phylogenetic tree plot annotated with metadata describing how many orthologous genes each species shares with the reference\_species ("human" by default).

#### Usage

```
plot_orthotree(
  tree = NULL,
  orth_report = NULL,
  species = NULL,
  method = c("homologene", "gprofiler", "babelgene"),
  tree_source = "timetree",
  non121_strategy = "drop_both_species",
  reference_species = "human",
  clades = list(Primates = c("Homo sapiens", "Macaca mulatta"), Eutherians =
   c("Homo sapiens", "Mus musculus", "Bos taurus"), Mammals = c("Homo sapiens",
  "Mus musculus", "Bos taurus", "Ornithorhynchus anatinus", "Monodelphis domestica"),
  Tetrapods = c("Homo sapiens", "Mus musculus", "Gallus gallus", "Anolis carolinensis",
    "Xenopus tropicalis"), Vertebrates = c("Homo sapiens", "Mus musculus",
   "Gallus gallus", "Anolis carolinensis", "Xenopus tropicalis", "Danio rerio")),
  scaling_factor = 1,
  show_plot = TRUE,
 save_paths = c(tempfile(fileext = ".ggtree.pdf"), tempfile(fileext = ".ggtree.png")),
  width = 10,
  height = 10,
  mc.cores = 1,
  verbose = TRUE
)
```

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#### **Arguments**

tree

A phylogenetic tree of class phylo. If no tree is provided (NULL) a 100-way multiz tree will be imported from UCSC Genome Browser.

orth\_report

An ortholog report from one or more species generated by report\_orthologs.

species

Species to include in the final plot. If NULL, then all species from the given database (method) will be included (via map\_species), so long as they also exist in the tree.

method

R package to use for gene mapping:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

tree\_source

Can be one of the following:

- "timetree2022": Import and prune the TimeTree >147k species phylogenetic tree. Can also simply type "timetree".
- "timetree2015": Import and prune the TimeTree >50k species phylogenetic tree.
- "OmaDB":

Construct a tree from OMA (Orthologous Matrix browser) via the getTaxonomy function. *NOTE:* Does not contain branch lengths, and therefore may have limited utility.

 "UCSC": Import and prune the UCSC 100-way alignment phylogenetic tree (hg38 version).

• "<path>":

Read a tree from a newick text file from a local or remote URL using read.tree.

non121\_strategy

How to handle genes that don't have 1:1 mappings between input\_species:output\_species. Options include:

- "drop\_both\_species" or "dbs" or 1:
   Drop genes that have duplicate mappings in either the input\_species or output\_species
   (DEFAULT).
- "drop\_input\_species" or "dis" or 2:
  Only drop genes that have duplicate mappings in the input\_species.
- "drop\_output\_species" or "dos" or 3:
  Only drop genes that have duplicate mappings in the output\_species.
- "keep\_both\_species" or "kbs" or 4:
   Keep all genes regardless of whether they have duplicate mappings in either species.
- "keep\_popular" or "kp" or 5: Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.

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• "sum", "mean", "median", "min" or "max":

When gene\_df is a matrix and gene\_output="rownames", these options
will aggregate many-to-one gene mappings (input\_species-to-output\_species)
after dropping any duplicate genes in the output\_species.

#### reference\_species

Reference species.

clades A named list of clades each containing list fo species to define the respective

clade using MRCA.

scaling\_factor How much to scale y-axis parameters (e.g. offset) by.

show\_plot Whether to print the final tree plot.

save\_paths Paths to save plot to.
width Saved plot width.
height Saved plot height.

mc.cores Number of cores to parallelise different steps with.

verbose Print messages.

#### Value

#### A list containing:

- plot: Annotated ggtree object.
- tree: The pruned, standardised phylogenetic tree used in the plot.
- orth\_report : Ortholog reports for each species against the reference\_species.
- metadata: Metadata used in the plot, including silhouette PNG ids from phylopic.
- clades : Metadata used for highlighting clades.
- method: method used.
- reference\_species : reference\_species used.
- save\_paths : save\_paths to plot.

## Source

ggtree tutorial

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prepare\_tree

Prepare a phylogenetic tree

#### **Description**

Import a phylogenetic tree and then conduct a series of optional standardisation steps. Optionally, if output\_format is not NULL, species names from both the tree and the species argument will first be standardised using map\_species.

# Usage

```
prepare_tree(
   tree_source = "timetree",
   species = NULL,
   output_format = "scientific_name",
   run_map_species = c(TRUE, TRUE),
   method = c("homologene", "gprofiler", "babelgene"),
   force_ultrametric = TRUE,
   age_max = NULL,
   show_plot = TRUE,
   verbose = TRUE,
   ...
)
```

# **Arguments**

tree\_source

Can be one of the following:

- "timetree2022": Import and prune the TimeTree >147k species phylogenetic tree. Can also simply type "timetree".
- "timetree2015": Import and prune the TimeTree >50k species phylogenetic tree.
- "OmaDB":

Construct a tree from OMA (Orthologous Matrix browser) via the getTaxonomy function. *NOTE:* Does not contain branch lengths, and therefore may have limited utility.

- "UCSC": Import and prune the UCSC 100-way alignment phylogenetic tree (hg38 version).
- "<path>":
   Read a tree from a newick text file from a local or remote URL using read.tree.

species Species names to subset the tree by (after standardise\_species step).

output\_format
run\_map\_species

Which column to return.

Whether to first standardise species names with map\_species.

method

R package to use for gene mapping:

• "gprofiler": Slower but more species and genes.

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- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

force\_ultrametric

Whether to force the tree to be ultrametric (i.e. make all tips the same date)

using force.ultrametric.

age\_max Rescale the edges of the tree into units of millions of years (MY) instead than

evolutionary rates (e.g.  $dN/dS\ ratios).$  Only used if  $age\_max,$  the  $max\ number$  ,

is numeric. Times are computed using makeChronosCalib and chronos.

show\_plot Show a basic plot of the resulting tree.

verbose Print messages.

... Additional arguments passed to makeChronosCalib.

#### Value

A filtered tree of class "phylo" (with standardised species names).

#### Source

# TimeTree 5: An Expanded Resource for Species Divergence Times

#### **Examples**

```
species <- c("human","chimp","mouse")
tr <- orthogene::prepare_tree(species = species)</pre>
```

report\_orthologs

Report orthologs

## **Description**

Identify the number of orthologous genes between two species.

# Usage

```
report_orthologs(
   target_species = "mouse",
   reference_species = "human",
   standardise_genes = FALSE,
   method_all_genes = c("homologene", "gprofiler", "babelgene"),
   method_convert_orthologs = method_all_genes,
   drop_nonorths = TRUE,
   non121_strategy = "drop_both_species",
   round_digits = 2,
   return_report = TRUE,
   mc.cores = 1,
   verbose = TRUE,
   ...
)
```

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#### **Arguments**

target\_species Target species.

reference\_species

Reference species.

standardise\_genes

If TRUE AND gene\_output="columns", a new column "input\_gene\_standard" will be added to gene\_df containing standardised HGNC symbols identified by gorth.

method\_all\_genes

R package to to use in all\_genes step:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

method\_convert\_orthologs

R package to to use in convert\_orthologs step:

- "gprofiler": Slower but more species and genes.
- "homologene": Faster but fewer species and genes.
- "babelgene": Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.

drop\_nonorths
non121\_strategy

Drop genes that don't have an ortholog in the output\_species.

How to handle genes that don't have 1:1 mappings between input\_species:output\_species. Options include:

- "drop\_both\_species" or "dbs" or 1:
   Drop genes that have duplicate mappings in either the input\_species or output\_species
   (DEFAULT).
- "drop\_input\_species" or "dis" or 2:
  Only drop genes that have duplicate mappings in the input\_species.
- "drop\_output\_species" or "dos" or 3:
  Only drop genes that have duplicate mappings in the output\_species.
- "keep\_both\_species" or "kbs" or 4:
   Keep all genes regardless of whether they have duplicate mappings in either species.
- "keep\_popular" or "kp" or 5: Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.
- "sum", "mean", "median", "min" or "max":

  When gene\_df is a matrix and gene\_output="rownames", these options
  will aggregate many-to-one gene mappings (input\_species-to-output\_species)
  after dropping any duplicate genes in the output\_species.

return\_report Return just the ortholog mapping between two species (FALSE) or return both the ortholog mapping as well a data. frame of the report statistics (TRUE).

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mc.cores Number of cores to parallelise each target\_species with.verbose Print messages.Additional arguments to be passed to gorth or homologene.

*NOTE*: To return only the most "popular" interspecies ortholog mappings, supply mthreshold=1 here AND set method="gprofiler" above. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.

For more details, please see here.

#### Value

A list containing:

- map: A table of inter-species gene mappings.
- report : A list of aggregate orthology report statistics.

If >1 target\_species are provided, then a table of aggregated report statistics concatenated across species will be returned instead.

```
orth_fly <- orthogene::report_orthologs(
   target_species = "fly",
   reference_species = "human"
)</pre>
```

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