

# Package: EWCE (via r-universe)

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**Type** Package

**Title** Expression Weighted Celltype Enrichment

**Version** 1.21.0

**Description** Used to determine which cell types are enriched within gene lists. The package provides tools for testing enrichments within simple gene lists (such as human disease associated genes) and those resulting from differential expression studies. The package does not depend upon any particular Single Cell Transcriptome dataset and user defined datasets can be loaded in and used in the analyses.

**URL** <https://github.com/NathanSkene/EWCE>

**BugReports** <https://github.com/NathanSkene/EWCE/issues>

**License** GPL-3

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EWCE-package*EWCE: Expression Weighted Celltype Enrichment*

---

## Description

Used to determine which cell types are enriched within gene lists. The package provides tools for testing enrichments within simple gene lists (such as human disease associated genes) and those resulting from differential expression studies. The package does not depend upon any particular Single Cell Transcriptome dataset and user defined datasets can be loaded in and used in the analyses.

## Details

EWCE: Expression Weighted Celltype Enrichment

Used to determine which cell types are enriched within gene lists. The package provides tools for testing enrichments within simple gene lists (such as human disease associated genes) and those resulting from differential expression studies.

The package does not depend upon any particular Single Cell Transcriptome dataset and user defined datasets can be loaded in and used in the analyses.

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## See Also

Useful links:

- <https://github.com/NathanSkene/EWCE>
- Report bugs at <https://github.com/NathanSkene/EWCE/issues>

---

```
add_res_to_merging_list
```

*Add to results to merging list*

---

## Description

add\_res\_to\_merging\_list adds EWCE results to a list for merging analysis.

## Usage

```
add_res_to_merging_list(full_res, existing_results = NULL)
```

## Arguments

|                  |                                                                                                                                                                                                                                                  |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| full_res         | Results list generated using <a href="#">bootstrap_enrichment_test</a> or <a href="#">ewce_expression_data</a> functions. Multiple results tables can be merged into one results table, as long as the 'list' column is set to distinguish them. |
| existing_results | Output of previous rounds from adding results to list. Leave empty if this is the first item in the list.                                                                                                                                        |

## Value

Merged results list.

## Examples

```
# Load the single cell data
ctd <- ewceData::ctd()

# Load the data
tt_alzh <- ewceData::tt_alzh()
# tt_alzh_BA36 <- ewceData::tt_alzh_BA36()
# Use 3 bootstrap lists for speed, for publishable analysis use >10000
reps <- 3
# Use 5 up/down regulated genes (thresh) for speed, default is 250
thresh <- 5
# Run EWCE analysis
# tt_results <- ewce_expression_data(
#   sct_data = ctd, tt = tt_alzh, annotLevel = 1, thresh = thresh,
#   reps = reps, ttSpecies = "human", sctSpecies = "mouse"
# )
# tt_results_36 <- ewce_expression_data(
#   sct_data = ctd, tt = tt_alzh_BA36, annotLevel = 1, thresh = thresh,
#   reps = reps, ttSpecies = "human", sctSpecies = "mouse"
# )

# Fill a list with the results
results <- add_res_to_merging_list(tt_alzh)
# results <- add_res_to_merging_list(tt_alzh_BA36, results)
```

---

```
bin_columns_into_quantiles
      bin_columns_into_quantiles
```

---

### Description

bin\_columns\_into\_quantiles is an internal function used to convert a vector of specificity into a vector of specificity quantiles. This function can be iterated across a matrix using [apply](#) to create a matrix of specificity quantiles.

### Usage

```
bin_columns_into_quantiles(
  vec,
  numberOfBins = 40,
  defaultBin = as.integer(numberOfBins/2)
)
```

### Arguments

|              |                                                                                                                                                                                                               |
|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| vec          | The vector of gene of specificity values.                                                                                                                                                                     |
| numberOfBins | Number of quantile bins to use (40 is recommended).                                                                                                                                                           |
| defaultBin   | Which bin to assign when there's only one non-zero quantile. In situations where there's only one non-zero quantile, <a href="#">cut</a> throws an error. Avoid these situations by using a default quantile. |

### Value

A vector with same length as vec but with columns storing quantiles instead of specificity.

### Examples

```
ctd <- ewceData::ctd()
ctd[[1]]$specificity_quantiles <- apply(ctd[[1]]$specificity, 2,
  FUN = bin_columns_into_quantiles)
```

---

```
bin_specificity_into_quantiles
      bin_specificity_into_quantiles
```

---

### Description

bin\_specificity\_into\_quantiles is an internal function used to convert add '\$specificity\_quantiles' to a ctd

**Usage**

```
bin_specificity_into_quantiles(
  ctdIN,
  numberOfBins,
  matrix_name = "specificity_quantiles",
  as_sparse = TRUE,
  verbose = TRUE
)
```

**Arguments**

|              |                                                                                              |
|--------------|----------------------------------------------------------------------------------------------|
| ctdIN        | A single annotLevel of a ctd, i.e. ctd[[1]] (the function is intended to be used via apply). |
| numberOfBins | Number of quantile 'bins' to use (40 is recommended).                                        |
| matrix_name  | Name of the specificity matrix to create (default: "specificity_quantiles").                 |
| as_sparse    | Convert to sparseMatrix.                                                                     |
| verbose      | Print messages.                                                                              |

**Value**

A ctd with "specificity\_quantiles" matrix in each level (or whatever matrix\_name was set to.).

**Examples**

```
ctd <- ewceData::ctd()
ctd <- lapply(ctd, EWCE::bin_specificity_into_quantiles, numberOfBins = 40)
print(ctd[[1]]$specificity_quantiles[1:3, ])
```

---

bootstrap\_enrichment\_test

*Bootstrap cell type enrichment test*


---

**Description**

bootstrap\_enrichment\_test takes a genelist and a single cell type transcriptome dataset and determines the probability of enrichment and fold changes for each cell type.

**Usage**

```
bootstrap_enrichment_test(
  sct_data = NULL,
  hits = NULL,
  bg = NULL,
  genelistSpecies = NULL,
  sctSpecies = NULL,
  sctSpecies_origin = sctSpecies,
```

```

output_species = "human",
method = "homologene",
reps = 100,
no_cores = 1,
annotLevel = 1,
geneSizeControl = FALSE,
controlledCT = NULL,
mtc_method = "BH",
sort_results = TRUE,
standardise_sct_data = TRUE,
standardise_hits = FALSE,
verbose = TRUE,
localHub = FALSE,
store_gene_data = TRUE
)

```

## Arguments

|                   |                                                                                                                                                                                                                                                                                          |
|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| sct_data          | List generated using <a href="#">generate_celltype_data</a> .                                                                                                                                                                                                                            |
| hits              | List of gene symbols containing the target gene list. Will automatically be converted to human gene symbols if geneSizeControl=TRUE.                                                                                                                                                     |
| bg                | List of gene symbols containing the background gene list (including hit genes). If bg=NULL, an appropriate gene background will be created automatically.                                                                                                                                |
| genelistSpecies   | Species that hits genes came from (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                           |
| sctSpecies        | Species that sct_data is currently formatted as (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                             |
| sctSpecies_origin | Species that the sct_data originally came from, regardless of its current gene format (e.g. it was previously converted from mouse to human gene orthologs). This is used for computing an appropriate background.                                                                       |
| output_species    | Species to convert sct_data and hits to (Default: "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                                                  |
| method            | R package to use for gene mapping:<br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources. |
| reps              | Number of random gene lists to generate ( <i>Default: 100</i> , but should be $\geq 10,000$ for publication-quality results).                                                                                                                                                            |
| no_cores          | Number of cores to parallelise bootstrapping reps over.                                                                                                                                                                                                                                  |
| annotLevel        | An integer indicating which level of sct_data to analyse ( <i>Default: 1</i> ).                                                                                                                                                                                                          |
| geneSizeControl   | Whether you want to control for GC content and transcript length. Recommended if the gene list originates from genetic studies ( <i>Default: FALSE</i> ). If set to TRUE, then hits must be from humans.                                                                                 |

|                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| controlledCT         | [Optional] If not NULL, and instead is the name of a cell type, then the bootstrapping controls for expression within that cell type.                                                                                                                                                                                                                                                                                                                                                                                           |
| mtc_method           | Multiple-testing correction method (passed to <a href="#">p.adjust</a> ).                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| sort_results         | Sort enrichment results from smallest to largest p-values.                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| standardise_sct_data | Should sct_data be standardised? if TRUE: <ul style="list-style-type: none"> <li>• When sctSpecies!=output_species the sct_data will be checked for object formatting and the genes will be converted to the orthologs of the output_species with <a href="#">standardise_ctd</a> (which calls <a href="#">map_genes</a> internally).</li> <li>• When sctSpecies==output_species, the sct_data will be checked for object formatting with <a href="#">standardise_ctd</a>, but the gene names will remain untouched.</li> </ul> |
| standardise_hits     | Should hits be standardised? If TRUE: <ul style="list-style-type: none"> <li>• When genelistSpecies!=output_species, the genes will be converted to the orthologs of the output_species with <a href="#">convert_orthologs</a>.</li> <li>• When genelistSpecies==output_species, the genes will be standardised with <a href="#">map_genes</a>.</li> </ul> <p>If FALSE, hits will be passed on to subsequent steps as-is.</p>                                                                                                   |
| verbose              | Print messages.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| localHub             | If working offline, add argument localHub=TRUE to work with a local, non-updated hub; It will only have resources available that have previously been downloaded. If offline, Please also see BiocManager vignette section on offline use to ensure proper functionality.                                                                                                                                                                                                                                                       |
| store_gene_data      | Store sampled gene data for every bootstrap iteration. When the number of bootstrap reps is very high ( $\geq 100k$ ) and/or the number of genes in hits is very high, you may want to set store_gene_data=FALSE to avoid using excessive amounts of CPU memory.                                                                                                                                                                                                                                                                |

## Value

A list containing three elements:

- hit.cells: vector containing the summed proportion of expression in each cell type for the target list.
- gene\_data: data.table showing the number of time each gene appeared in the bootstrap sample.
- bootstrap\_data: matrix in which each row represents the summed proportion of expression in each cell type for one of the random lists
- controlledCT: the controlled cell type (if applicable)

**Examples**

```
# Load the single cell data
sct_data <- ewceData::ctd()
# Set the parameters for the analysis
# Use 3 bootstrap lists for speed, for publishable analysis use >=10,000
reps <- 3
# Load gene list from Alzheimer's disease GWAS
hits <- ewceData::example_genelist()

# Bootstrap significance test, no control for transcript length or GC content
full_results <- EWCE::bootstrap_enrichment_test(
  sct_data = sct_data,
  hits = hits,
  reps = reps,
  annotLevel = 1,
  sctSpecies = "mouse",
  genelistSpecies = "human")
```

---

```
check_ewce_genelist_inputs
      check_ewce_genelist_inputs
```

---

**Description**

check\_ewce\_genelist\_inputs Is used to check that hits and bg gene lists passed to EWCE are setup correctly. Checks they are the appropriate length. Checks all hits are in bg. Checks the species match and if not reduces to 1:1 orthologs.

**Usage**

```
check_ewce_genelist_inputs(
  sct_data,
  hits,
  bg = NULL,
  genelistSpecies = NULL,
  sctSpecies = NULL,
  sctSpecies_origin = sctSpecies,
  output_species = "human",
  method = "homologene",
  geneSizeControl = FALSE,
  standardise_sct_data = TRUE,
  standardise_hits = FALSE,
  min_genes = 4,
  verbose = TRUE
)
```

**Arguments**

|                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| sct_data             | List generated using <a href="#">generate_celltype_data</a> .                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| hits                 | List of gene symbols containing the target gene list. Will automatically be converted to human gene symbols if <code>geneSizeControl=TRUE</code> .                                                                                                                                                                                                                                                                                                                                                                                                    |
| bg                   | List of gene symbols containing the background gene list (including hit genes). If <code>bg=NULL</code> , an appropriate gene background will be created automatically.                                                                                                                                                                                                                                                                                                                                                                               |
| genelistSpecies      | Species that hits genes came from (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                                                                                                                                                                                                                                                                                        |
| sctSpecies           | Species that sct_data is currently formatted as (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                                                                                                                                                                                                                                                                          |
| sctSpecies_origin    | Species that the sct_data originally came from, regardless of its current gene format (e.g. it was previously converted from mouse to human gene orthologs). This is used for computing an appropriate background.                                                                                                                                                                                                                                                                                                                                    |
| output_species       | Species to convert sct_data and hits to (Default: "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                                                                                                                                                                                                                                                                                                               |
| method               | R package to use for gene mapping:<br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.                                                                                                                                                                                                                                                              |
| geneSizeControl      | Whether you want to control for GC content and transcript length. Recommended if the gene list originates from genetic studies ( <i>Default: FALSE</i> ). If set to TRUE, then hits must be from humans.                                                                                                                                                                                                                                                                                                                                              |
| standardise_sct_data | Should sct_data be standardised? if TRUE: <ul style="list-style-type: none"> <li>When <code>sctSpecies!=output_species</code> the sct_data will be checked for object formatting and the genes will be converted to the orthologs of the output_species with <a href="#">standardise_ctd</a> (which calls <a href="#">map_genes</a> internally).</li> <li>When <code>sctSpecies==output_species</code>, the sct_data will be checked for object formatting with <a href="#">standardise_ctd</a>, but the gene names will remain untouched.</li> </ul> |
| standardise_hits     | Should hits be standardised? If TRUE: <ul style="list-style-type: none"> <li>When <code>genelistSpecies!=output_species</code>, the genes will be converted to the orthologs of the output_species with <a href="#">convert_orthologs</a>.</li> <li>When <code>genelistSpecies==output_species</code>, the genes will be standardised with <a href="#">map_genes</a>.</li> </ul> <p>If FALSE, hits will be passed on to subsequent steps as-is.</p>                                                                                                   |
| min_genes            | Minimum number of genes in a gene list to test.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| verbose              | Print messages.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

**Value**

A list containing

- hits: Array of MGI/HGNC gene symbols containing the target gene list.
- bg: Array of MGI/HGNC gene symbols containing the background gene list.

**Examples**

```
ctd <- ewceData::ctd()
example_genelist <- ewceData::example_genelist()

# Called from "bootstrap_enrichment_test()" and "generate_bootstrap_plots()"
checkedLists <- EWCE::check_ewce_genelist_inputs(
  sct_data = ctd,
  hits = example_genelist,
  sctSpecies = "mouse",
  genelistSpecies = "human"
)
```

---

|                    |                                                |
|--------------------|------------------------------------------------|
| check_percent_hits | <i>Get percentage of target cell type hits</i> |
|--------------------|------------------------------------------------|

---

**Description**

After you run [bootstrap\\_enrichment\\_test](#), check what percentage of significantly enriched cell types match an expected cell type.

**Usage**

```
check_percent_hits(
  full_results,
  target_celltype,
  mtc_method = "bonferroni",
  q_threshold = 0.05,
  verbose = TRUE
)
```

**Arguments**

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| full_results    | bootstrap_enrichment_test results.                             |
| target_celltype | Substring to search to matching cell types (case-insensitive). |
| mtc_method      | Multiple-testing correction method.                            |
| q_threshold     | Corrected significance threshold.                              |
| verbose         | Print messages.                                                |

**Value**

Report list.

**Examples**

```
## Bootstrap significance test,  
## no control for transcript length or GC content  
## Use pre-computed results to speed up example  
full_results <- EWCE::example_bootstrap_results()  
  
report <- EWCE::check_percent_hits(  
  full_results = full_results,  
  target_celltype = "microglia"  
)
```

---

controlled\_geneset\_enrichment

*Celltype controlled geneset enrichment*

---

**Description**

controlled\_geneset\_enrichment tests whether a functional gene set is still enriched in a disease gene set after controlling for the disease gene set's enrichment in a particular cell type (the 'controlledCT')

**Usage**

```
controlled_geneset_enrichment(  
  disease_genes,  
  functional_genes,  
  bg = NULL,  
  sct_data,  
  sctSpecies = NULL,  
  output_species = "human",  
  disease_genes_species = NULL,  
  functional_genes_species = NULL,  
  method = "homologene",  
  annotLevel,  
  reps = 100,  
  controlledCT,  
  use_intersect = FALSE,  
  verbose = TRUE  
)
```

**Arguments**

|                          |                                                                                                                                                                                                                                                                                          |
|--------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| disease_genes            | Array of gene symbols containing the disease gene list. Does not have to be disease genes. Must be from same species as the single cell transcriptome dataset.                                                                                                                           |
| functional_genes         | Array of gene symbols containing the functional gene list. The enrichment of this gene set within the disease_genes is tested. Must be from same species as the single cell transcriptome dataset.                                                                                       |
| bg                       | List of gene symbols containing the background gene list (including hit genes). If bg=NULL, an appropriate gene background will be created automatically.                                                                                                                                |
| sct_data                 | List generated using <a href="#">generate_celltype_data</a> .                                                                                                                                                                                                                            |
| sctSpecies               | Species that sct_data is currently formatted as (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                             |
| output_species           | Species to convert sct_data and hits to (Default: "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                                                  |
| disease_genes_species    | Species of the disease_genes gene set.                                                                                                                                                                                                                                                   |
| functional_genes_species | Species of the functional_genes gene set.                                                                                                                                                                                                                                                |
| method                   | R package to use for gene mapping:<br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources. |
| annotLevel               | An integer indicating which level of sct_data to analyse ( <i>Default: 1</i> ).                                                                                                                                                                                                          |
| reps                     | Number of random gene lists to generate ( <i>Default: 100</i> , but should be $\geq 10,000$ for publication-quality results).                                                                                                                                                            |
| controlledCT             | [Optional] If not NULL, and instead is the name of a cell type, then the bootstrapping controls for expression within that cell type.                                                                                                                                                    |
| 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.                                                                                            |
| verbose                  | Print messages.                                                                                                                                                                                                                                                                          |

**Value**

A list containing three data frames:

- **p\_controlled** The probability that functional\_genes are enriched in disease\_genes while controlling for the level of specificity in controlledCT
- **z\_controlled** The z-score that functional\_genes are enriched in disease\_genes while controlling for the level of specificity in controlledCT
- **p\_uncontrolled** The probability that functional\_genes are enriched in disease\_genes WITHOUT controlling for the level of specificity in controlledCT

- `z_uncontrolled` The z-score that functional\_genes are enriched in disease\_genes WITHOUT controlling for the level of specificity in controlledCT
- `reps=reps`
- `controlledCT`
- `actualOverlap=actual` The number of genes that overlap between functional and disease gene sets

## Examples

```
# See the vignette for more detailed explanations
# Gene set enrichment analysis controlling for cell type expression
# set seed for bootstrap reproducibility
set.seed(12345678)
## load merged dataset from vignette
ctd <- ewceData::ctd()
schiz_genes <- ewceData::schiz_genes()
hpsd_genes <- ewceData::hpsd_genes()
# Use 3 bootstrap lists for speed, for publishable analysis use >10000
reps <- 3

res_hpsd_schiz <- EWCE::controlled_geneset_enrichment(
  disease_genes = schiz_genes,
  functional_genes = hpsd_genes,
  sct_data = ctd,
  annotLevel = 1,
  reps = reps,
  controlledCT = "pyramidal CA1"
)
```

---

ctd\_to\_sce

---

*CellTypeDataset to SingleCellExperiment*


---

## Description

Copied from [scKirby](#), which is not yet on CRAN or Bioconductor.

## Usage

```
ctd_to_sce(object, as_sparse = TRUE, as_DelayedArray = FALSE, verbose = TRUE)
```

## Arguments

|                              |                                                      |
|------------------------------|------------------------------------------------------|
| <code>object</code>          | CellTypeDataset object.                              |
| <code>as_sparse</code>       | Store SingleCellExperiment matrices as sparse.       |
| <code>as_DelayedArray</code> | Store SingleCellExperiment matrices as DelayedArray. |
| <code>verbose</code>         | Print messages.                                      |

**Value**

SingleCellExperiment

**Examples**

```
ctd <- ewceData::ctd()
sce <- EWCE::ctd_to_sce(ctd)
```

---

drop\_uninformative\_genes

*Drop uninformative genes*

---

**Description**

drop\_uninformative\_genes drops uninformative genes in order to reduce compute time and noise in subsequent steps. It achieves this through several steps, each of which are optional:

- Drop non-1:1 orthologs:  
Removes genes that don't have 1:1 orthologs with the output\_species ("human" by default).
- Drop non-varying genes:  
Removes genes that don't vary across cells based on variance deciles.
- Drop non-differentially expressed genes (DEGs):  
Removes genes that are not significantly differentially expressed across cell-types (multiple DEG methods available).

**Usage**

```
drop_uninformative_genes(  
  exp,  
  level2annot,  
  mtc_method = "BH",  
  adj_pval_thresh = 1e-05,  
  convert_orths = FALSE,  
  input_species = NULL,  
  output_species = "human",  
  non121_strategy = "drop_both_species",  
  method = "homologene",  
  as_sparse = TRUE,  
  as_DelayedArray = FALSE,  
  return_sce = FALSE,  
  no_cores = 1,  
  verbose = TRUE,  
  ...  
)
```

**Arguments**

|                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| exp             | Expression matrix with gene names as rownames.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| level2annot     | Array of cell types, with each sequentially corresponding a column in the expression matrix.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| mtc_method      | Multiple-testing correction method used by DGE step. See <a href="#">p.adjust</a> for more details.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| adj_pval_thresh | Minimum differential expression significance that a gene must demonstrate across level2annot (i.e. cell types).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| convert_orths   | If input_species!=output_species and convert_orths=TRUE, will drop genes without 1:1 output_species orthologs and then convert exp gene names to those of output_species.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| input_species   | Which species the gene names in exp come from. See <a href="#">list_species</a> for all available species.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| output_species  | Which species' genes names to convert exp to. See <a href="#">list_species</a> for all available species.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| non121_strategy | How to handle genes that don't have 1:1 mappings between input_species:output_species. Options include:<br><br>"drop_both_species" or "dbs" or 1 Drop genes that have duplicate mappings in either the input_species or output_species ( <i>DEFAULT</i> ).<br>"drop_input_species" or "dis" or 2 Only drop genes that have duplicate mappings in the input_species.<br>"drop_output_species" or "dos" or 3 Only drop genes that have duplicate mappings in the output_species.<br>"keep_both_species" or "kbs" or 4 Keep all genes regardless of whether they have duplicate mappings in either species.<br>"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.<br>"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. |
| method          | R package to use for gene mapping:<br><br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| as_sparse       | Convert exp to sparse matrix.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| as_DelayedArray | Convert exp to DelayedArray for scalable processing.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

return\_sce Whether to return the filtered results as an expression matrix or a **SingleCellExperiment**.  
 no\_cores Number of cores to parallelise across. Set to NULL to automatically optimise.  
 verbose Print messages. #' @inheritParams orthogene::convert\_orthologs  
 ... Arguments passed on to [orthogene::convert\\_orthologs](#)  
 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. or tibble.  
     list 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".  
 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](#).  
 drop\_nonorths Drop genes that don't have an ortholog 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).  
 sort\_rows Sort gene\_df rows alphanumerically.  
 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 inter-species gene aggregation/expansion.

gene\_map=NULL **and** input\_species==output\_species A gene\_map is automatically generated by [map\\_genes](#) to perform within-species 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.

### Value

exp Expression matrix with gene names as row names.

### Examples

```
cortex_mrna <- ewceData::cortex_mrna()
# Use only a subset of genes to keep the example quick
cortex_mrna$exp <- cortex_mrna$exp[1:300, ]

## Convert orthologs at the same time
exp2_orth <- drop_uninformative_genes(
  exp = cortex_mrna$exp,
  level2annot = cortex_mrna$annot$level2class,
  input_species = "mouse"
)
```

---

ewce\_expression\_data    *Bootstrap cell type enrichment test for transcriptome data*

---

### Description

ewce\_expression\_data takes a differential gene expression (DGE) results table and determines the probability of cell type enrichment in the up- and down- regulated genes.

### Usage

```
ewce_expression_data(
  sct_data,
  annotLevel = 1,
  tt,
  sortBy = "t",
  thresh = 250,
  reps = 100,
```

```

    ttSpecies = NULL,
    sctSpecies = NULL,
    output_species = NULL,
    bg = NULL,
    method = "homologene",
    verbose = TRUE,
    localHub = FALSE
)

```

## Arguments

|                |                                                                                                                                                                                                                                                                                          |
|----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| sct_data       | List generated using <a href="#">generate_celltype_data</a> .                                                                                                                                                                                                                            |
| annotLevel     | An integer indicating which level of sct_data to analyse ( <i>Default: 1</i> ).                                                                                                                                                                                                          |
| tt             | Differential expression table. Can be output of <a href="#">topTable</a> function. Minimum requirement is that one column stores a metric of increased/decreased expression (i.e. log fold change, t-statistic for differential expression etc) and another contains gene symbols.       |
| sortBy         | Column name of metric in tt which should be used to sort up- from down-regulated genes ( <i>Default: "t"</i> ).                                                                                                                                                                          |
| thresh         | The number of up- and down- regulated genes to be included in each analysis ( <i>Default: 250</i> ).                                                                                                                                                                                     |
| reps           | Number of random gene lists to generate ( <i>Default: 100</i> , but should be $\geq 10,000$ for publication-quality results).                                                                                                                                                            |
| ttSpecies      | The species the differential expression table was generated from.                                                                                                                                                                                                                        |
| sctSpecies     | Species that sct_data is currently formatted as (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                             |
| output_species | Species to convert sct_data and hits to ( <i>Default: "human"</i> ). See <a href="#">list_species</a> for all available species.                                                                                                                                                         |
| bg             | List of gene symbols containing the background gene list (including hit genes). If bg=NULL, an appropriate gene background will be created automatically.                                                                                                                                |
| method         | R package to use for gene mapping:<br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources. |
| verbose        | Print messages.                                                                                                                                                                                                                                                                          |
| localHub       | If working offline, add argument localHub=TRUE to work with a local, non-updated hub; It will only have resources available that have previously been downloaded. If offline, Please also see BiocManager vignette section on offline use to ensure proper functionality.                |

## Value

A list containing five data frames:

- `results`: dataframe in which each row gives the statistics (p-value, fold change and number of standard deviations from the mean) associated with the enrichment of the stated cell type in the gene list. An additional column `*Direction*` stores whether it the result is from the up or downregulated set.
- `hit.cells.up`: vector containing the summed proportion of expression in each cell type for the target list.
- `hit.cells.down`: vector containing the summed proportion of expression in each cell type for the target list.
- `bootstrap_data.up`: matrix in which each row represents the summed proportion of expression in each cell type for one of the random lists.
- `bootstrap_data.down`: matrix in which each row represents the summed proportion of expression in each cell type for one of the random lists.

## Examples

```
# Load the single cell data
ctd <- ewceData::ctd()

# Set the parameters for the analysis
# Use 3 bootstrap lists for speed, for publishable analysis use >10000
reps <- 3
# Use 5 up/down regulated genes (thresh) for speed, default is 250
thresh <- 5
annotLevel <- 1 # <- Use cell level annotations (i.e. Interneurons)

# Load the top table
tt_alzh <- ewceData::tt_alzh()

tt_results <- EWCE::ewce_expression_data(
  sct_data = ctd,
  tt = tt_alzh,
  annotLevel = 1,
  thresh = thresh,
  reps = reps,
  ttSpecies = "human",
  sctSpecies = "mouse"
)
```

---

ewce\_plot

*Plot EWCE results*


---

## Description

`ewce_plot` generates plots of EWCE enrichment results

**Usage**

```
ewce_plot(
  total_res,
  mtc_method = "bonferroni",
  q_threshold = 0.05,
  ctd = NULL,
  annotLevel = 1,
  heights = c(0.3, 1),
  make_dendro = FALSE,
  verbose = TRUE
)
```

**Arguments**

|             |                                                                                                                                                                                                                                                                                                                               |
|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| total_res   | Results data.frame generated using <a href="#">bootstrap_enrichment_test</a> or <a href="#">ewce_expression_data</a> functions. Multiple results tables can be merged into one results table, as long as the 'list' column is set to distinguish them. Multiple testing correction is then applied across all merged results. |
| mtc_method  | Method to be used for multiple testing correction. Argument is passed to <a href="#">p.adjust</a> (DEFAULT: "bonferroni").                                                                                                                                                                                                    |
| q_threshold | Corrected significance threshold.                                                                                                                                                                                                                                                                                             |
| ctd         | CellTypeDataset object. Should be provided so that the dendrogram can be taken from it and added to plots.                                                                                                                                                                                                                    |
| annotLevel  | An integer indicating which level of ctd to analyse ( <i>Default: 1</i> ).                                                                                                                                                                                                                                                    |
| heights     | The relative heights row in the grid. Will get repeated to match the dimensions of the grid. Passed to <a href="#">wrap_plots</a> .                                                                                                                                                                                           |
| make_dendro | Add a dendrogram (requires ctd).                                                                                                                                                                                                                                                                                              |
| verbose     | Print messages.                                                                                                                                                                                                                                                                                                               |

**Value**

A named list containing versions of the [ggplot](#) with and without the dendrogram. Note that cell type order on the x-axis is based on hierarchical clustering for both plots if make\_dendro = TRUE.

**Examples**

```
## Bootstrap significance test,
## no control for transcript length or GC content
## Use pre-computed results to speed up example
total_res <- EWCE::example_bootstrap_results()$results
plt <- ewce_plot(total_res = total_res)
```

---

example\_bootstrap\_results

*Example bootstrap enrichment results*


---

## Description

Example cell type enrichment results produced by [bootstrap\\_enrichment\\_test](#).

## Usage

```
example_bootstrap_results(verbose = TRUE, localHub = FALSE)
```

## Arguments

|          |                                                                                                                                                                                                                                                                           |
|----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| verbose  | Print messages.                                                                                                                                                                                                                                                           |
| localHub | If working offline, add argument localHub=TRUE to work with a local, non-updated hub; It will only have resources available that have previously been downloaded. If offline, Please also see BiocManager vignette section on offline use to ensure proper functionality. |

## Value

List with 3 items.

## Source

```
# Load the single cell data
ctd <- ewceData::ctd()
# Set the parameters for the analysis
# Use 3 bootstrap lists for speed, for publishable analysis use >=10,000
reps <- 3
# Load gene list from Alzheimer's disease GWAS
example_genelist <- ewceData::example_genelist()
# Bootstrap significance test, no control for transcript length or GC content
full_results <- EWCE::bootstrap_enrichment_test( sct_data = ctd, hits = example_genelist, reps =
reps, annotLevel = 1, sctSpecies = "mouse", genelistSpecies = "human" )
bootstrap_results <- full_results
save(bootstrap_results,file = "inst/extdata/bootstrap_results.rda")
```

## Examples

```
full_results <- example_bootstrap_results()
```

---

`example_transcriptome_results`*Example bootstrap celltype enrichment test for transcriptome data*

---

**Description**

Example celltype enrichment results produced by [ewce\\_expression\\_data](#).

**Usage**

```
example_transcriptome_results(verbose = TRUE, localHub = FALSE)
```

**Arguments**

|                       |                                                                                                                                                                                                                                                                                        |
|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>verbose</code>  | Print messages.                                                                                                                                                                                                                                                                        |
| <code>localHub</code> | If working offline, add argument <code>localHub=TRUE</code> to work with a local, non-updated hub; It will only have resources available that have previously been downloaded. If offline, Please also see BiocManager vignette section on offline use to ensure proper functionality. |

**Value**

List with 5 items.

**Source**

```
## Load the single cell data
ctd <- ewceData::ctd()
## Set the parameters for the analysis
## Use 3 bootstrap lists for speed, for publishable analysis use >10,000
reps <- 3
annotLevel <- 1 # <- Use cell level annotations (i.e. Interneurons)
## Use 5 up/down regulated genes (thresh) for speed, default is 250
thresh <- 5
## Load the top table
tt_alzh <- ewceData::tt_alzh()
tt_results <- EWCE::ewce_expression_data( sct_data = ctd, tt = tt_alzh, annotLevel = 1, thresh =
thresh, reps = reps, ttSpecies = "human", sctSpecies = "mouse" )
save(tt_results, file = "inst/extdata/tt_results.rda")
```

**Examples**

```
tt_results <- EWCE::example_transcriptome_results()
```

---

|                  |                                          |
|------------------|------------------------------------------|
| filter_ctd_genes | <i>Filter genes in a CellTypeDataset</i> |
|------------------|------------------------------------------|

---

**Description**

Removes rows from each matrix within a CellTypeDataset (CTD) that are not within gene\_subset.

**Usage**

```
filter_ctd_genes(ctd, gene_subset)
```

**Arguments**

|             |                     |
|-------------|---------------------|
| ctd         | CellTypeDataset.    |
| gene_subset | Genes to subset to. |

**Value**

Filtered CellTypeDataset.

**Examples**

```
ctd <- ewceData::ctd()
ctd <- standardise_ctd(ctd, input_species="mouse")
gene_subset <- rownames(ctd[[1]]$mean_exp)[1:100]
ctd_subset <- EWCE::filter_ctd_genes(ctd = ctd, gene_subset = gene_subset)
```

---

|                                   |                                          |
|-----------------------------------|------------------------------------------|
| filter_genes_without_1to1_homolog | <i>filter_genes_without_1to1_homolog</i> |
|-----------------------------------|------------------------------------------|

---

**Description**

Deprecated function. Please use [filter\\_nonorthologs](#) instead.

**Usage**

```
filter_genes_without_1to1_homolog(
  filenames,
  input_species = "mouse",
  convert_nonhuman_genes = TRUE,
  annot_levels = NULL,
  suffix = "_orthologs",
  verbose = TRUE
)
```

**Arguments**

|                        |                                                             |
|------------------------|-------------------------------------------------------------|
| filenames              | List of file names for sct_data saved as <i>.rda</i> files. |
| input_species          | Which species the gene names in exp come from.              |
| convert_nonhuman_genes | Whether to convert the exp row names to human gene names.   |
| annot_levels           | [Optional] Names of each annotation level.                  |
| suffix                 | Suffix to add to the file name (right before <i>.rda</i> ). |
| verbose                | Print messages.                                             |

**Details**

**Note:** This function replaces the original filter\_genes\_without\_1to1\_homolog function. filter\_genes\_without\_1to1 is now a wrapper for filter\_nonorthologs.

**Value**

List of the filtered CellTypeData file names.

**Examples**

```
# Load the single cell data
ctd <- ewceData::ctd()
tmp <- tempfile()
save(ctd, file = tmp)
fNames_ALLCELLS_orths <- EWCE::filter_nonorthologs(filenames = tmp)
```

---

|                     |                             |
|---------------------|-----------------------------|
| filter_nonorthologs | <i>Filter non-orthologs</i> |
|---------------------|-----------------------------|

---

**Description**

filter\_nonorthologs Takes the filenames of CellTypeData files, loads them, drops any genes which don't have a 1:1 orthologs with humans, and then convert the gene to human orthologs. The new files are then saved to disk, appending '\_orthologs' to the file name.

**Usage**

```
filter_nonorthologs(
  filenames,
  input_species = NULL,
  convert_nonhuman_genes = TRUE,
  annot_levels = NULL,
  suffix = "_orthologs",
  method = "homologene",
  non121_strategy = "drop_both_species",
  verbose = TRUE,
  ...
)
```

**Arguments**

|                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| filenames              | List of file names for sct_data saved as <i>.rda</i> files.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| input_species          | Which species the gene names in exp come from.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| convert_nonhuman_genes | Whether to convert the exp row names to human gene names.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| annot_levels           | [Optional] Names of each annotation level.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| suffix                 | Suffix to add to the file name (right before <i>.rda</i> ).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| method                 | R package to use for gene mapping:<br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| non121_strategy        | How to handle genes that don't have 1:1 mappings between input_species:output_species. Options include:<br><br>"drop_both_species" or "dbs" or 1 Drop genes that have duplicate mappings in either the input_species or output_species ( <i>DEFAULT</i> ).<br>"drop_input_species" or "dis" or 2 Only drop genes that have duplicate mappings in the input_species.<br>"drop_output_species" or "dos" or 3 Only drop genes that have duplicate mappings in the output_species.<br>"keep_both_species" or "kbs" or 4 Keep all genes regardless of whether they have duplicate mappings in either species.<br>"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.<br>"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.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| ...                    | Arguments passed on to <a href="#">orthogene::convert_orthologs</a>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| gene_df                | Data object containing the genes (see gene_input for options on how the genes can be stored within the object).<br>Can be one of the following formats:<br><br>matrix A sparse or dense matrix.<br>data.frame A data.frame, data.table. or tibble.<br>list A list or character vector.<br><br>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".

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](#).

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

drop\_nonorths Drop genes that don't have an ortholog 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.

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 inter-species gene aggregation/expansion.

gene\_map=NULL **and** input\_species==output\_species A gene\_map is automatically generated by [map\\_genes](#) to perform within-species 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.

### Details

**Note:** This function replaces the original filter\_genes\_without\_1to1\_homolog function. filter\_genes\_without\_1to1 is now a wrapper for filter\_nonorthologs.

### Value

List of the filtered CellTypeData file names.

### Examples

```
# Load the single cell data
ctd <- ewceData::ctd()
tmp <- tempfile()
save(ctd, file = tmp)
fNames_ALLCELLS_orths <- EWCE::filter_nonorthologs(filenamees = tmp)
```

---

fix\_bad\_hgnc\_symbols    *fix\_bad\_hgnc\_symbols*

---

### Description

Given an expression matrix, wherein the rows are supposed to be HGNC symbols, find those symbols which are not official HGNC symbols, then correct them if possible. Return the expression matrix with corrected symbols.

### Usage

```
fix_bad_hgnc_symbols(
  exp,
  dropNonHGNC = FALSE,
  as_sparse = TRUE,
  verbose = TRUE,
  localHub = FALSE
)
```

**Arguments**

|             |                                                                                                                                                                                                                                                                           |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| exp         | An expression matrix where the rows are HGNC symbols or a SingleCellExperiment (SCE) or other Ranged Summarized Experiment (SE) type object.                                                                                                                              |
| dropNonHGNC | Boolean. Should symbols not recognised as HGNC symbols be dropped?                                                                                                                                                                                                        |
| as_sparse   | Convert exp to sparse matrix.                                                                                                                                                                                                                                             |
| verbose     | Print messages.                                                                                                                                                                                                                                                           |
| localHub    | If working offline, add argument localHub=TRUE to work with a local, non-updated hub; It will only have resources available that have previously been downloaded. If offline, Please also see BiocManager vignette section on offline use to ensure proper functionality. |

**Value**

Returns the expression matrix with the rownames corrected and rows representing the same gene merged. If a SingleCellExperiment (SCE) or other Ranged Summarized Experiment (SE) type object was inputted this will be returned with the corrected expression matrix under counts.

**Examples**

```
# create example expression matrix, could be part of a exp, annot list obj
exp <- matrix(data = runif(70), ncol = 10)
# Add HGNC gene names but add with an error:
# MARCH8 is a HGNC symbol which if opened in excel will convert to Mar-08
rownames(exp) <-
  c("MT-TF", "MT-RNR1", "MT-TV", "MT-RNR2", "MT-TL1", "MT-ND1", "Mar-08")
exp <- fix_bad_hgnc_symbols(exp)
# fix_bad_hgnc_symbols warns the user of this possible issue
```

---

|                     |                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| fix_bad_mgi_symbols | <i>fix_bad_mgi_symbols - Given an expression matrix, wherein the rows are supposed to be MGI symbols, find those symbols which are not official MGI symbols, then check in the MGI synonym database for whether they match to a proper MGI symbol. Where a symbol is found to be an aliases for a gene that is already in the dataset, the combined reads are summed together.</i> |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

---

**Description**

Also checks whether any gene names contain "Sep", "Mar" or "Feb". These should be checked for any suggestion that excel has corrupted the gene names.

**Usage**

```
fix_bad_mgi_symbols(
  exp,
  mrk_file_path = NULL,
  printAllBadSymbols = FALSE,
  as_sparse = TRUE,
  verbose = TRUE,
  localHub = FALSE
)
```

**Arguments**

|                    |                                                                                                                                                                                                                                                                           |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| exp                | An expression matrix where the rows are MGI symbols, or a SingleCellExperiment (SCE) or other Ranged Summarized Experiment (SE) type object.                                                                                                                              |
| mrk_file_path      | Path to the MRK_List2 file which can be downloaded from <a href="http://www.informatics.jax.org/downloads/reports/in">www.informatics.jax.org/downloads/reports/in</a>                                                                                                    |
| printAllBadSymbols | Output to console all the bad gene symbols                                                                                                                                                                                                                                |
| as_sparse          | Convert exp to sparse matrix.                                                                                                                                                                                                                                             |
| verbose            | Print messages.                                                                                                                                                                                                                                                           |
| localHub           | If working offline, add argument localHub=TRUE to work with a local, non-updated hub; It will only have resources available that have previously been downloaded. If offline, Please also see BiocManager vignette section on offline use to ensure proper functionality. |

**Value**

Returns the expression matrix with the rownames corrected and rows representing the same gene merged. If no corrections are necessary, input expression matrix is returned. If a SingleCellExperiment (SCE) or other Ranged Summarized Experiment (SE) type object was inputted this will be returned with the corrected expression matrix under counts.

**Examples**

```
# Load the single cell data
cortex_mrna <- ewceData::cortex_mrna()
# take a subset for speed
cortex_mrna$exp <- cortex_mrna$exp[1:50, 1:5]
cortex_mrna$exp <- fix_bad_mgi_symbols(cortex_mrna$exp)
```

---

|                    |                           |
|--------------------|---------------------------|
| fix_celltype_names | <i>Fix celltype names</i> |
|--------------------|---------------------------|

---

**Description**

Make sure celltypes don't contain characters that could interfere with downstream analyses. For example, the R package **MAGMA.Celltyping** cannot have spaces in celltype names because spaces are used as a delimiter in later steps.

**Usage**

```
fix_celltype_names(
  celltypes,
  replace_chars = "[~][.][ ]|[//]|[\\/]\"",
  make_unique = TRUE
)
```

**Arguments**

celltypes      Character vector of celltype names.

replace\_chars    Regex string of characters to replace with "\_" when renaming columns.

make\_unique      Make all entries unique.

**Value**

Fixed celltype names.

**Examples**

```
ct <- c("microglia", "astoryocytes", "Pyramidal SS")
ct_fixed <- fix_celltype_names(celltypes = ct)
```

---

```
generate_bootstrap_plots
      Generate bootstrap plots
```

---

**Description**

generate\_bootstrap\_plots takes a gene list and a single cell type transcriptome dataset and generates plots which show how the expression of the genes in the list compares to those in randomly generated gene lists.

**Usage**

```
generate_bootstrap_plots(
  sct_data = NULL,
  hits = NULL,
  bg = NULL,
  genelistSpecies = NULL,
  sctSpecies = NULL,
  output_species = "human",
  method = "homologene",
  reps = 100,
  annotLevel = 1,
  geneSizeControl = FALSE,
  full_results = NULL,
```

```

listFileName = paste0("_level", annotLevel),
adj_pval_thresh = 0.05,
facets = "CellType",
scales = "free_x",
save_dir = file.path(tempdir(), "BootstrapPlots"),
show_plot = TRUE,
verbose = TRUE
)

```

## Arguments

|                 |                                                                                                                                                                                                                                                                                          |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| sct_data        | List generated using <a href="#">generate_celltype_data</a> .                                                                                                                                                                                                                            |
| hits            | List of gene symbols containing the target gene list. Will automatically be converted to human gene symbols if <code>geneSizeControl=TRUE</code> .                                                                                                                                       |
| bg              | List of gene symbols containing the background gene list (including hit genes). If <code>bg=NULL</code> , an appropriate gene background will be created automatically.                                                                                                                  |
| genelistSpecies | Species that hits genes came from (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                           |
| sctSpecies      | Species that sct_data is currently formatted as (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                             |
| output_species  | Species to convert sct_data and hits to (Default: "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                                                  |
| method          | R package to use for gene mapping:<br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources. |
| reps            | Number of random gene lists to generate ( <i>Default: 100</i> , but should be $\geq 10,000$ for publication-quality results).                                                                                                                                                            |
| annotLevel      | An integer indicating which level of sct_data to analyse ( <i>Default: 1</i> ).                                                                                                                                                                                                          |
| geneSizeControl | Whether you want to control for GC content and transcript length. Recommended if the gene list originates from genetic studies ( <i>Default: FALSE</i> ). If set to TRUE, then hits must be from humans.                                                                                 |
| full_results    | The full output of <a href="#">bootstrap_enrichment_test</a> for the same gene list.                                                                                                                                                                                                     |
| listFileName    | String used as the root for files saved using this function.                                                                                                                                                                                                                             |
| adj_pval_thresh | Adjusted p-value threshold of celltypes to include in plots.                                                                                                                                                                                                                             |
| facets          | <b>[Deprecated]</b> Please use rows and cols instead.                                                                                                                                                                                                                                    |
| scales          | Are scales shared across all facets (the default, "fixed"), or do they vary across rows ("free_x"), columns ("free_y"), or both rows and columns ("free")?                                                                                                                               |
| save_dir        | Directory where the BootstrapPlots folder should be saved, default is a temp directory.                                                                                                                                                                                                  |
| show_plot       | Print the plot.                                                                                                                                                                                                                                                                          |
| verbose         | Print messages.                                                                                                                                                                                                                                                                          |

**Value**

Saves a set of pdf files containing graphs and returns the file where they are saved. These will be saved with the file name adjusted using the value of `listFileName`. The files are saved into the 'BootstrapPlot' folder. Files start with one of the following:

- `qqplot_noText`: sorts the gene list according to how enriched it is in the relevant cell type. Plots the value in the target list against the mean value in the bootstrapped lists.
- `qqplot_wtGSym`: as above but labels the gene symbols for the highest expressed genes.
- `bootDists`: rather than just showing the mean of the bootstrapped lists, a boxplot shows the distribution of values
- `bootDists_LOG`: shows the bootstrapped distributions with the y-axis shown on a log scale

**Examples**

```
## Load the single cell data
sct_data <- ewceData::ctd()

## Set the parameters for the analysis
## Use 5 bootstrap lists for speed, for publishable analysis use >10000
reps <- 5

## Load the gene list and get human orthologs
hits <- ewceData::example_genelist()

## Bootstrap significance test,
## no control for transcript length or GC content
## Use pre-computed results to speed up example
full_results <- EWCE::example_bootstrap_results()

### Skip this for example purposes
# full_results <- EWCE::bootstrap_enrichment_test(
#   sct_data = sct_data,
#   hits = hits,
#   reps = reps,
#   annotLevel = 1,
#   sctSpecies = "mouse",
#   genelistSpecies = "human"
# )

output <- EWCE::generate_bootstrap_plots(
  sct_data = sct_data,
  hits = hits,
  reps = reps,
  full_results = full_results,
  sctSpecies = "mouse",
  genelistSpecies = "human",
  annotLevel = 1
)
```

---

```
generate_bootstrap_plots_for_transcriptome
```

*Generate bootstrap plots*

---

## Description

Takes a gene list and a single cell type transcriptome dataset and generates plots which show how the expression of the genes in the list compares to those in randomly generated gene lists.

## Usage

```
generate_bootstrap_plots_for_transcriptome(
  sct_data,
  tt,
  bg = NULL,
  thresh = 250,
  annotLevel = 1,
  reps = 100,
  full_results = NA,
  listFileName = "",
  showGNameThresh = 25,
  ttSpecies = NULL,
  sctSpecies = NULL,
  output_species = NULL,
  sortBy = "t",
  sig_only = TRUE,
  sig_col = "q",
  sig_thresh = 0.05,
  celltype_col = "CellType",
  plot_types = c("bootstrap", "bootstrap_distributions", "log_bootstrap_distributions"),
  save_dir = file.path(tempdir(), "BootstrapPlots"),
  method = "homologene",
  verbose = TRUE
)
```

## Arguments

|          |                                                                                                                                                                                                                                                                                    |
|----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| sct_data | List generated using <a href="#">generate_celltype_data</a> .                                                                                                                                                                                                                      |
| tt       | Differential expression table. Can be output of <a href="#">topTable</a> function. Minimum requirement is that one column stores a metric of increased/decreased expression (i.e. log fold change, t-statistic for differential expression etc) and another contains gene symbols. |
| bg       | List of gene symbols containing the background gene list (including hit genes). If bg=NULL, an appropriate gene background will be created automatically.                                                                                                                          |
| thresh   | The number of up- and down- regulated genes to be included in each analysis (Default: 250).                                                                                                                                                                                        |

|                 |                                                                                                                                                                                                                                                                                          |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| annotLevel      | An integer indicating which level of sct_data to analyse ( <i>Default: 1</i> ).                                                                                                                                                                                                          |
| reps            | Number of random gene lists to generate ( <i>Default: 100</i> , but should be $\geq 10,000$ for publication-quality results).                                                                                                                                                            |
| full_results    | The full output of <a href="#">ewce_expression_data</a> for the same gene list.                                                                                                                                                                                                          |
| listFileName    | String used as the root for files saved using this function.                                                                                                                                                                                                                             |
| showGNameThresh | Integer. If a gene has over X percent of it's expression proportion in a cell type, then list the gene name.                                                                                                                                                                             |
| ttSpecies       | The species the differential expression table was generated from.                                                                                                                                                                                                                        |
| sctSpecies      | Species that sct_data is currently formatted as (no longer limited to just "mouse" and "human"). See <a href="#">list_species</a> for all available species.                                                                                                                             |
| output_species  | Species to convert sct_data and hits to (Default: "human"). See <a href="#">list_species</a> for all available species.                                                                                                                                                                  |
| sortBy          | Column name of metric in tt which should be used to sort up- from down-regulated genes (Default: "t").                                                                                                                                                                                   |
| sig_only        | Should plots only be generated for cells which have significant changes?                                                                                                                                                                                                                 |
| sig_col         | Column name in tt that contains the significance values.                                                                                                                                                                                                                                 |
| sig_thresh      | Threshold by which to filter tt by sig_col.                                                                                                                                                                                                                                              |
| celltype_col    | Column within tt that contains celltype names.                                                                                                                                                                                                                                           |
| plot_types      | Plot types to generate.                                                                                                                                                                                                                                                                  |
| save_dir        | Directory where the BootstrapPlots folder should be saved, default is a temp directory.                                                                                                                                                                                                  |
| method          | R package to use for gene mapping:<br>"gprofiler" Slower but more species and genes.<br>"homologene" Faster but fewer species and genes.<br>"babelgene" Faster but fewer species and genes. Also gives consensus scores for each gene mapping based on a several different data sources. |
| verbose         | Print messages.                                                                                                                                                                                                                                                                          |

## Value

Saves a set of PDF files containing graphs. Then returns a nested list with each plot and the path where it was saved to. Files start with one of the following:

- qqplot\_noText: sorts the gene list according to how enriched it is in the relevant cell type. Plots the value in the target list against the mean value in the bootstrapped lists.
- qqplot\_wtGSym: as above but labels the gene symbols for the highest expressed genes.
- bootDists: rather than just showing the mean of the bootstrapped lists, a boxplot shows the distribution of values
- bootDists\_LOG: shows the bootstrapped distributions with the y-axis shown on a log scale

**Examples**

```
## Load the single cell data
ctd <- ewceData::ctd()

## Set the parameters for the analysis
## Use 3 bootstrap lists for speed, for publishable analysis use >10,000
reps <- 3
annotLevel <- 1 # <- Use cell level annotations (i.e. Interneurons)
## Use 5 up/down regulated genes (thresh) for speed, default is 250
thresh <- 5

## Load the top table
tt_alzh <- ewceData::tt_alzh()

## See ?example_transcriptome_results for full code to produce tt_results
tt_results <- EWCE::example_transcriptome_results()

## Bootstrap significance test,
## no control for transcript length or GC content
savePath <- EWCE::generate_bootstrap_plots_for_transcriptome(
  sct_data = ctd,
  tt = tt_alzh,
  thresh = thresh,
  annotLevel = 1,
  full_results = tt_results,
  listFileName = "examples",
  reps = reps,
  ttSpecies = "human",
  sctSpecies = "mouse",
  # Only do one plot type for demo purposes
  plot_types = "bootstrap"
)
```

---

generate\_celltype\_data

*Generate CellTypeData (CTD) file*

---

**Description**

generate\_celltype\_data takes gene expression data and cell type annotations and creates Cell-TypeData (CTD) files which contain matrices of mean expression and specificity per cell type.

**Usage**

```
generate_celltype_data(
  exp,
  annotLevels,
  groupName,
  no_cores = 1,
```

```

    savePath = tempdir(),
    file_prefix = "ctd",
    as_sparse = TRUE,
    as_DelayedArray = FALSE,
    normSpec = FALSE,
    convert_orths = FALSE,
    input_species = "mouse",
    output_species = "human",
    non121_strategy = "drop_both_species",
    method = "homologene",
    force_new_file = TRUE,
    specificity_quantiles = TRUE,
    numberOfBins = 40,
    dendrograms = TRUE,
    return_ctd = FALSE,
    verbose = TRUE,
    ...
)

```

### Arguments

|                 |                                                                                                                                                                                     |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| exp             | Numerical matrix with row for each gene and column for each cell. Row names are gene symbols. Column names are cell IDs which can be cross referenced against the annot data frame. |
| annotLevels     | List with arrays of strings containing the cell type names associated with each column in exp.                                                                                      |
| groupName       | A human readable name for referring to the dataset being used.                                                                                                                      |
| no_cores        | Number of cores that should be used to speedup the computation. <i>NOTE:</i> Use no_cores=1 when using this package in windows system.                                              |
| savePath        | Directory where the CTD file should be saved.                                                                                                                                       |
| file_prefix     | Prefix to add to saved CTD file name.                                                                                                                                               |
| as_sparse       | Convert exp to a sparse Matrix.                                                                                                                                                     |
| as_DelayedArray | Convert exp to DelayedArray.                                                                                                                                                        |
| normSpec        | Boolean indicating whether specificity data should be transformed to a normal distribution by cell type, giving equivalent scores across all cell types.                            |
| convert_orths   | If input_species!=output_species and convert_orths=TRUE, will drop genes without 1:1 output_species orthologs and then convert exp gene names to those of output_species.           |
| input_species   | The species that the exp dataset comes from. See <a href="#">list_species</a> for all available species.                                                                            |
| output_species  | Species to convert exp to (Default: "human"). See <a href="#">list_species</a> for all available species.                                                                           |
| 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.

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.

force\_new\_file If a file of the same name as the one being created already exists, overwrite it.

specificity\_quantiles Compute specificity quantiles. Recommended to set to TRUE.

numberOfBins Number of quantile 'bins' to use (40 is recommended).

dendrograms Add dendrogram plots

return\_ctd Return the CTD object in a list along with the file name, instead of just the file name.

verbose Print messages.

... Arguments passed on to [orthogene::convert\\_orthologs](#)

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. or tibble.

list 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".  
 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](#).  
 drop\_nonorths Drop genes that don't have an ortholog 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).  
 sort\_rows Sort gene\_df rows alphanumerically.  
 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 inter-species gene aggregation/expansion.  
 gene\_map=NULL **and** input\_species==output\_species A gene\_map is automatically generated by [map\\_genes](#) to perform within-species 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.

## Value

File names for the saved CellTypeData (CTD) files.

## Examples

```
# Load the single cell data
cortex_mrna <- ewceData::cortex_mrna()
```

```
# Use only a subset to keep the example quick
expData <- cortex_mrna$exp[1:100, ]
l1 <- cortex_mrna$annot$level1class
l2 <- cortex_mrna$annot$level2class
annotLevels <- list(l1 = l1, l2 = l2)
fNames_ALLCELLS <- EWCE::generate_celltype_data(
  exp = expData,
  annotLevels = annotLevels,
  groupName = "allKImouse"
)
```

---

|                                 |                           |
|---------------------------------|---------------------------|
| <code>get_celltype_table</code> | <i>get_celltype_table</i> |
|---------------------------------|---------------------------|

---

## Description

`get_celltype_table` Generates a table that can be used for supplementary tables of publications. The table lists how many cells are associated with each cell type, the level of annotation, and the dataset from which it was generated.

## Usage

```
get_celltype_table(annot)
```

## Arguments

|                    |                                                                                              |
|--------------------|----------------------------------------------------------------------------------------------|
| <code>annot</code> | An annotation dataframe, which columns named 'level1class', 'level2class' and 'dataset_name' |
|--------------------|----------------------------------------------------------------------------------------------|

## Value

A dataframe with columns 'name', 'level', 'freq' and 'dataset\_name'

## Examples

```
# See PrepLDSC.Rmd for origin of merged_ALLCELLS$annot
cortex_mrna <- ewceData::cortex_mrna()
cortex_mrna$annot$dataset_name <- "cortex_mrna"
celltype_table <- EWCE::get_celltype_table(cortex_mrna$annot)
```

---

|                  |                                             |
|------------------|---------------------------------------------|
| is_delayed_array | Assess whether an object is a DelayedArray. |
|------------------|---------------------------------------------|

---

**Description**

Assess whether an object is a DelayedArray or one of its derived object types.

**Usage**

```
is_delayed_array(X)
```

**Arguments**

X                      Object.

**Value**

boolean

---

|           |                                      |
|-----------|--------------------------------------|
| is_matrix | Assess whether an object is a Matrix |
|-----------|--------------------------------------|

---

**Description**

Assess whether an object is a Matrix or one of its derived object types.

**Usage**

```
is_matrix(X)
```

**Arguments**

X                      Object.

**Value**

boolean

---

|                  |                                                    |
|------------------|----------------------------------------------------|
| is_sparse_matrix | <i>Assess whether an object is a sparse matrix</i> |
|------------------|----------------------------------------------------|

---

**Description**

Assess whether an object is a sparse matrix or one of its derived object types.

**Usage**

```
is_sparse_matrix(X)
```

**Arguments**

X                      Object.

**Value**

boolean

---

|              |                         |
|--------------|-------------------------|
| list_species | <i>List all species</i> |
|--------------|-------------------------|

---

**Description**

List all species that EWCE can convert genes from/to. Wrapper function for [map\\_species](#).

**Usage**

```
list_species(verbose = TRUE)
```

**Arguments**

verbose                Print messages.

**Value**

List of species EWCE can input/output genes as.

**Examples**

```
list_species()
```

---

|            |            |
|------------|------------|
| load_rdata | load_rdata |
|------------|------------|

---

**Description**

Load processed data (.rda format) using a function that assigns it to a specific variable (so you don't have to guess what the loaded variable name is).

**Usage**

```
load_rdata(fileName)
```

**Arguments**

|          |                           |
|----------|---------------------------|
| fileName | Name of the file to load. |
|----------|---------------------------|

**Value**

Data object.

**Examples**

```
tmp <- tempfile()
save(mtcars, file = tmp)
mtcars2 <- load_rdata(tmp)
```

---

|           |                                                  |
|-----------|--------------------------------------------------|
| merge_ctd | <i>Merge multiple CellTypeDataset references</i> |
|-----------|--------------------------------------------------|

---

**Description**

Import CellTypeDataset (CTD) references from a remote repository, standardize each, and then merge into one CTD. Optionally, can return these as a merged [SingleCellExperiment](#).

**Usage**

```
merge_ctd(
  CTD_list,
  save_dir = tempdir(),
  standardise_CTD = FALSE,
  as_SCE = FALSE,
  gene_union = TRUE,
  merge_levels = seq(1, 5),
  save_split_SCE = FALSE,
  save_split_CTD = FALSE,
  save_merged_SCE = TRUE,
```

```

    force_new_quantiles = FALSE,
    numberOfBins = 40,
    as_sparse = TRUE,
    as_DelayedArray = FALSE,
    verbose = TRUE,
    ...
)

```

## Arguments

|                     |                                                                                                                                                                                                                                                                          |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| CTD_list            | (Named) list of CellTypeDatasets.                                                                                                                                                                                                                                        |
| save_dir            | The directory to save merged files in.                                                                                                                                                                                                                                   |
| standardise_CTD     | Whether to run <code>standardise_ctd</code> .                                                                                                                                                                                                                            |
| as_SCE              | If TRUE (default), returns the merged results as a named list of <a href="#">SingleCellExperiments</a> . If FALSE, returns as a CTD object.                                                                                                                              |
| gene_union          | Whether to take the gene union or intersection when merging matrices (mean_exp, specificity, etc.).                                                                                                                                                                      |
| merge_levels        | Which CTD levels you want to merge. Can be a single value (e.g. <code>merge_levels=5</code> ) or a list c(e.g. <code>merge_levels=c(1:5)</code> ). If some CTD don't have the same number of levels, the maximum level depth available in that CTD will be used instead. |
| save_split_SCE      | Whether to save individual SCE files in the subdirectory <i>standardized_CTD_SCE</i> .                                                                                                                                                                                   |
| save_split_CTD      | Whether to save individual CTD files in the subdirectory <i>standardized_CTD</i> .                                                                                                                                                                                       |
| save_merged_SCE     | Save the final merged SCE object, or simply to return it.                                                                                                                                                                                                                |
| force_new_quantiles | If specificity quantiles matrix already exists, create a new one.                                                                                                                                                                                                        |
| numberOfBins        | Number of bins to compute specificity quantiles with.                                                                                                                                                                                                                    |
| as_sparse           | Convert matrices to sparse matrix.                                                                                                                                                                                                                                       |
| as_DelayedArray     | Convert matrices to DelayedArray.                                                                                                                                                                                                                                        |
| verbose             | Print messages.                                                                                                                                                                                                                                                          |
| ...                 | Additional arguments to be passed to <code>standardise_ctd</code> .                                                                                                                                                                                                      |

## Value

List of CellTypeDatasets or SingleCellExperiments.

## Examples

```

## Let's pretend these are different CTD datasets
ctd1 <- ewceData::ctd()
ctd2 <- ctd1
CTD_list <- list(ctd1, ctd2)
CTD_merged <- EWCE::merge_ctd(CTD_list = CTD_list)

```

---

merge\_sce*Merge multiple SingleCellExperiment objects*

---

**Description**

Merge several SingleCellExperiment (SCE) objects from different batches/experiments. Extracted from the **scMerge** package.

**Usage**

```
merge_sce(  
  sce_list,  
  method = "intersect",  
  cut_off_batch = 0.01,  
  cut_off_overall = 0.01,  
  use_assays = NULL,  
  colData_names = NULL,  
  batch_names = NULL,  
  verbose = TRUE  
)
```

**Arguments**

|                 |                                                                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| sce_list        | A list contains the SingleCellExperiment Object from each batch.                                                                                          |
| method          | A string indicates the method of combining the gene expression matrix, either union or intersect. Default to intersect. union only supports matrix class. |
| cut_off_batch   | A numeric vector indicating the cut-off for the proportion of a gene is expressed within each batch.                                                      |
| cut_off_overall | A numeric vector indicating the cut-off for the proportion of a gene is expressed overall data.                                                           |
| use_assays      | A string vector indicating the expression matrices to be combined. The first assay named will be used to determine the proportion of zeros.               |
| colData_names   | A string vector indicating the colData that are combined.                                                                                                 |
| batch_names     | A string vector indicating the batch names for the output SCE object.                                                                                     |
| verbose         | Print messages.                                                                                                                                           |

**Value**

A SingleCellExperiment object with the list of SCE objects combined.

**Author(s)**

Yingxin Lin (modified by Brian Schilder)

**Source**

[scMerge](#).

**Examples**

```

ctd <- ewceData::ctd()
sce_list <- EWCE::ctd_to_sce(object = ctd)
sce_combine <- merge_sce(sce_list = sce_list)

```

---

|                    |                            |
|--------------------|----------------------------|
| merge_two_expfiles | <i>Merge two exp files</i> |
|--------------------|----------------------------|

---

**Description**

merge\_two\_expfiles Used to combine two single cell type datasets.

**Usage**

```

merge_two_expfiles(
  exp1,
  exp2,
  annot1,
  annot2,
  name1 = "",
  name2 = "",
  as_sparse = TRUE,
  as_DelayedArray = FALSE,
  verbose = TRUE
)

```

**Arguments**

|           |                                                                                                                                                                                                             |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| exp1      | Numerical expression matrix for dataset1 with row for each gene and column for each cell. Row names are gene symbols. Column names are cell IDs which can be cross referenced against the annot data frame. |
| exp2      | Numerical expression matrix for dataset2 with row for each gene and column for each cell. Row names are gene symbols. Column names are cell IDs which can be cross referenced against the annot data frame. |
| annot1    | Annotation data frame for dataset1 which contains three columns at least: cell_id, level1class and level2class                                                                                              |
| annot2    | Annotation data frame for dataset2 which contains three columns at least: cell_id, level1class and level2class                                                                                              |
| name1     | Name used to refer to dataset 1. Leave blank if it's already a merged dataset.                                                                                                                              |
| name2     | Name used to refer to dataset 2. Leave blank if it's already a merged dataset.                                                                                                                              |
| as_sparse | Convert the merged exp to a sparse matrix.                                                                                                                                                                  |

as\_DelayedArray  
Convert the merged exp to a DelayedArray.

verbose  
Print messages.

**Value**

List containing merged exp and annot.

**Examples**

```
cortex_mrna <- ewceData::cortex_mrna()
exp1 <- cortex_mrna$exp[, 1:50]
exp2 <- cortex_mrna$exp[, 51:100]
annot1 <- cortex_mrna$annot[1:50, ]
annot2 <- cortex_mrna$annot[51:100, ]
merged_res <- EWCE::merge_two_expfiles(
  exp1 = exp1,
  exp2 = exp2,
  annot1 = annot1,
  annot2 = annot2,
  name1 = "dataset1",
  name2 = "dataset2"
)
```

merged\_ewce

*Multiple EWCE results from multiple studies***Description**

merged\_ewce combines enrichment results from multiple studies targetting the same scientific problem

**Usage**

```
merged_ewce(results, reps = 100)
```

**Arguments**

results      a list of EWCE results generated using [add\\_res\\_to\\_merging\\_list](#).

reps          Number of random gene lists to generate (Default=100 but should be >=10,000 for publication-quality results).

**Value**

dataframe in which each row gives the statistics (p-value, fold change and number of standard deviations from the mean) associated with the enrichment of the stated cell type in the gene list.

## Examples

```
# Load the single cell data
ctd <- ewceData::ctd()

# Use 3 bootstrap lists for speed, for publishable analysis use >10000
reps <- 3
# Use 5 up/down regulated genes (thresh) for speed, default is 250
thresh <- 5

# Load the data
tt_alzh_BA36 <- ewceData::tt_alzh_BA36()
tt_alzh_BA44 <- ewceData::tt_alzh_BA44()

# Run EWCE analysis
tt_results_36 <- EWCE::ewce_expression_data(
  sct_data = ctd,
  tt = tt_alzh_BA36,
  thresh = thresh,
  annotLevel = 1,
  reps = reps,
  ttSpecies = "human",
  sctSpecies = "mouse"
)
tt_results_44 <- EWCE::ewce_expression_data(
  sct_data = ctd,
  tt = tt_alzh_BA44,
  thresh = thresh,
  annotLevel = 1,
  reps = reps,
  ttSpecies = "human",
  sctSpecies = "mouse"
)

# Fill a list with the results
results <- EWCE::add_res_to_merging_list(tt_results_36)
results <- EWCE::add_res_to_merging_list(tt_results_44, results)

# Perform the merged analysis
# For publication reps should be higher
merged_res <- EWCE::merged_ewce(
  results = results,
  reps = 2
)
print(merged_res)
```

---

plot\_ctd

---

*Plot CellTypeData metrics*


---

## Description

Plot *CellTypeData* metrics such as mean\_exp, specificity and/or specificity\_quantiles.

**Usage**

```
plot_ctd(ctd, genes, level = 1, metric = "specificity", show_plot = TRUE)
```

**Arguments**

|           |                                                                                                                                                             |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ctd       | CellTypeDataset.                                                                                                                                            |
| genes     | Which genes in ctd to plot.                                                                                                                                 |
| level     | Annotation level in ctd to plot.                                                                                                                            |
| metric    | Which metric in the ctd to plot: <ul style="list-style-type: none"> <li>• "mean_exp"</li> <li>• "specificity"</li> <li>• "specificity_quantiles"</li> </ul> |
| show_plot | Whether to print the plot or simply return it.                                                                                                              |

**Value**

ggplot object.

**Examples**

```
ctd <- ewceData::ctd()
plt <- EWCE::plot_ctd(ctd, genes = c("Apoe", "Gfap", "Gapdh"))
```

---

|             |                    |
|-------------|--------------------|
| prep.dendro | <i>prep.dendro</i> |
|-------------|--------------------|

---

**Description**

prep\_dendro adds a dendrogram to a CellTypeDataset (CTD).

**Usage**

```
prep.dendro(ctdIN)
```

**Arguments**

|       |                                                                                              |
|-------|----------------------------------------------------------------------------------------------|
| ctdIN | A single annotLevel of a ctd, i.e. ctd[[1]] (the function is intended to be used via apply). |
|-------|----------------------------------------------------------------------------------------------|

**Value**

A CellTypeDataset with dendrogram plotting info added.

---

|               |                                    |
|---------------|------------------------------------|
| sct_normalize | <i>Normalize expression matrix</i> |
|---------------|------------------------------------|

---

### Description

Normalize expression matrix by accounting for library size. Uses **sctransform**.

### Usage

```
sct_normalize(exp, as_sparse = TRUE, verbose = TRUE)
```

### Arguments

|           |                                |
|-----------|--------------------------------|
| exp       | Gene x cell expression matrix. |
| as_sparse | Convert exp to sparse matrix.  |
| verbose   | Print messages.                |

### Value

Normalised expression matrix.

### Examples

```
cortex_mrna <- ewceData::cortex_mrna()
exp_sct_normed <- EWCE::sct_normalize(exp = cortex_mrna$exp[1:300, ])
```

---

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| standardise_ctd | <i>Convert a CellTypeDataset into standardized format</i> |
|-----------------|-----------------------------------------------------------|

---

### Description

This function will take a CTD, drop all genes without 1:1 orthologs with the output\_species ("human" by default), convert the remaining genes to gene symbols, assign names to each level, and convert all matrices to sparse matrices and/or DelayedArray.

### Usage

```
standardise_ctd(
  ctd,
  dataset,
  input_species = NULL,
  output_species = "human",
  sctSpecies_origin = input_species,
  non121_strategy = "drop_both_species",
  method = "homologene",
```

```

    force_new_quantiles = TRUE,
    force_standardise = FALSE,
    remove_unlabeled_clusters = FALSE,
    numberOfBins = 40,
    keep_annot = TRUE,
    keep_plots = TRUE,
    as_sparse = TRUE,
    as_DelayedArray = FALSE,
    rename_columns = TRUE,
    make_columns_unique = FALSE,
    verbose = TRUE,
    ...
)

```

## Arguments

|                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ctd               | Input CellTypeData.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| dataset           | CellTypeData. name.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| input_species     | Which species the gene names in exp come from. See <a href="#">list_species</a> for all available species.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| output_species    | Which species' genes names to convert exp to. See <a href="#">list_species</a> for all available species.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| sctSpecies_origin | Species that the sct_data originally came from, regardless of its current gene format (e.g. it was previously converted from mouse to human gene orthologs). This is used for computing an appropriate background.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| non121_strategy   | How to handle genes that don't have 1:1 mappings between input_species:output_species. Options include: <ul style="list-style-type: none"> <li>"drop_both_species" or "dbs" or 1 Drop genes that have duplicate mappings in either the input_species or output_species (<i>DEFAULT</i>).</li> <li>"drop_input_species" or "dis" or 2 Only drop genes that have duplicate mappings in the input_species.</li> <li>"drop_output_species" or "dos" or 3 Only drop genes that have duplicate mappings in the output_species.</li> <li>"keep_both_species" or "kbs" or 4 Keep all genes regardless of whether they have duplicate mappings in either species.</li> <li>"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.</li> <li>"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.</li> </ul> |
| 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.

**force\_new\_quantiles**  
 By default, quantile computation is skipped if they have already been computed. Set =TRUE to override this and generate new quantiles.

**force\_standardise**  
 If ctd has already been standardised, whether to rerun standardisation anyway (Default: FALSE).

**remove\_unlabeled\_clusters**  
 Remove any samples that have numeric column names.

**numberOfBins** Number of non-zero quantile bins.

**keep\_annot** Keep the column annotation data if provided.

**keep\_plots** Keep the dendrograms if provided.

**as\_sparse** Convert to sparse matrix.

**as\_DelayedArray**  
 Convert to DelayedArray.

**rename\_columns** Remove replace\_chars from column names.

**make\_columns\_unique**  
 Rename each columns with the prefix dataset.species.celltype.

**verbose** Print messages. Set verbose=2 if you want to print all messages from internal functions as well.

**...** Arguments passed on to [orthogene:convert\\_orthologs](#)

**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. or tibble.  
 list 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".

**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](#).

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

agg\_fun Aggregation function passed to [aggregate\\_mapped\\_genes](#). Set to NULL to skip aggregation step (default).

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

sort\_rows Sort gene\_df rows alphanumerically.

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 inter-species gene aggregation/expansion.

gene\_map=NULL **and** input\_species==output\_species A gene\_map is automatically generated by [map\\_genes](#) to perform within-species 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.

## Value

Standardised CellTypeDataset.

## Examples

```
ctd <- ewceData::ctd()
ctd_std <- EWCE::standardise_ctd(
  ctd = ctd,
  input_species = "mouse",
  dataset = "Zeisel2016"
)
```

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