

Package ‘TaxSEA’

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Type Package

Title Taxon Set Enrichment Analysis

Version 1.4.0

Description TaxSEA is an R package for Taxon Set Enrichment Analysis, which utilises a Kolmogorov-Smirnov test analyses to investigate differential abundance analysis output for whether there are alternations in a-priori defined sets of taxa from public databases (BugSigDB, MiMeDB, GutMGene, mBodyMap, BacDive and GMRepoV2) and collated from the literature. TaxSEA takes as input a list of taxonomic identifiers (e.g. species names, NCBI IDs etc.) and a rank (E.g. fold change, correlation coefficient). TaxSEA be applied to any microbiota taxonomic profiling technology (array-based, 16S rRNA gene sequencing, shotgun metagenomics & metatranscriptomics etc.) and enables researchers to rapidly contextualize their findings within the broader literature to accelerate interpretation of results.

License GPL-3

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biocViews Microbiome, Metagenomics, Sequencing, GeneSetEnrichment, RNASeq

URL <https://github.com/feargalr/taxsea>,
<https://feargalr.github.io/TaxSEA/>

BugReports <https://github.com/feargalr/taxsea/issues>

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get_ncbi_taxon_ids	<i>Retrieve NCBI Taxonomy IDs for a list of taxon names</i>
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Description

This function takes a vector of taxon names and returns a vector of NCBI taxonomy IDs by querying the NCBI Entrez API.

Usage

```
get_ncbi_taxon_ids(taxon_names)
```

Arguments

taxon_names A character vector of taxon names

Value

A character vector of NCBI taxonomy IDs corresponding to the input taxon names

Examples

```
taxon_names <- c("Escherichia coli", "Staphylococcus aureus")
taxon_ids <- get_ncbi_taxon_ids(taxon_names)
```

`get_taxon_sets`*Retrieve Taxon Sets from TaxSEA Library*

Description

Retrieve from the TaxSEA database which taxon sets (metabolite producers and disease signatures) contain a taxon of interest.

Usage

```
get_taxon_sets(taxon_to_fetch = taxon)
```

Arguments

`taxon_to_fetch` The taxon to search for in the TaxSEA database.

Value

A character vector containing the names of taxonomic sets where the specified taxon is present.

Examples

```
# Retrieve sets for Bifidobacterium longum
get_taxon_sets(taxon="Bifidobacterium_longum")
```

`NCBI_ids`*NCBI IDs Dataset*

Description

A dataset for mapping NCBI IDs to species/genus names. This named vector allows for lookup of NCBI IDs associated with species or genus names.

Usage

```
NCBI_ids
```

Format

A named vector where:

names NCBI IDs

values Species or genus names

A named vector mapping NCBI IDs to species or genus names.

Source

NCBI

Examples

```
data(NCBI_ids)
# Can look up either with or without spaces
NCBI_ids["Bifidobacterium_breve"]
NCBI_ids["Bifidobacterium breve"]
```

ssTaxSEA

Single-Sample Taxon Set Enrichment Analysis

Description

Computes per-sample enrichment scores for taxon sets using an ssGSEA-style approach. Counts are CLR-transformed, then each taxon is z-scored across samples to capture between-sample variation. Per-sample enrichment is then computed by ranking each sample's z-scores and applying a weighted running-sum statistic against taxon sets from the TaxSEA database.

Usage

```
ssTaxSEA(
  counts,
  lookup_missing = FALSE,
  min_set_size = 5,
  max_set_size = 300,
  custom_db = NULL
)
```

Arguments

counts	A numeric matrix, data.frame, or SummarizedExperiment/TreeSummarizedExperiment object. For matrix/data.frame input: rows are taxa, columns are samples, and row names must be taxon names (e.g. species names or NCBI IDs). For SummarizedExperiment input: the first assay is used and rownames() provide taxon identifiers.
lookup_missing	Logical indicating whether to fetch missing NCBI IDs via the NCBI API. Default is FALSE.

<code>min_set_size</code>	Minimum size of taxon sets to include. Default is 5.
<code>max_set_size</code>	Maximum size of taxon sets to include. Default is 300.
<code>custom_db</code>	A user-provided list of taxon sets. If NULL (default), the built-in TaxSEA database is used (excluding BugSigDB).

Details

The approach works as follows:

1. Raw counts are CLR-transformed (centered log-ratio with pseudocount of 0.5 for zeros).
2. Each taxon is then z-scored across all samples, so that values represent how much higher or lower a taxon is in a given sample relative to the cohort mean.
3. For each sample, the z-scores are ranked and an ssGSEA-style weighted running-sum enrichment score is computed for each taxon set.
4. A KS test p-value is also computed per sample per set.

This cohort-relative approach ensures that taxon sets which are consistently elevated in a subset of samples (e.g. disease samples) will produce high enrichment scores in those samples, even if the taxa are not the most abundant within any single sample.

Value

A list with two elements:

scores A matrix (samples x taxon sets) of enrichment scores. Positive scores indicate the set taxa tend to have higher abundance in that sample relative to the cohort.

pvalues A matrix (samples x taxon sets) of KS test p-values for each sample-set combination.

Examples

```
## Not run:
# From a count matrix (taxa x samples)
counts <- matrix(rpois(500, lambda = 10), nrow = 50, ncol = 10)
rownames(counts) <- paste0("Taxon_", seq_len(50))
colnames(counts) <- paste0("Sample_", seq_len(10))
res <- ssTaxSEA(counts, custom_db = list(
  set1 = paste0("Taxon_", 1:10),
  set2 = paste0("Taxon_", 20:30)
), min_set_size = 2)
head(res$scores)
head(res$pvalues)

## End(Not run)
```

taxon_rank_sets	<i>Taxon Rank Set Enrichment Analysis</i>
-----------------	---

Description

Groups species by taxonomic ranks and performs TaxSEA enrichment analysis at each rank level. Returns a named list of data frames, one per taxonomic rank (excluding species).

Usage

```
taxon_rank_sets(taxon_ranks, lineage_df, min_set_size = 5, max_set_size = 100)
```

Arguments

taxon_ranks	A named numeric vector of log2 fold changes. Names should be feature identifiers matching the species column in lineage_df, or matching rownames() of a SummarizedExperiment/TreeSummarizedExperiment.
lineage_df	Either a data frame or a SummarizedExperiment/TreeSummarizedExperiment object. Data frame input: Must include a species column and one or more taxonomic rank columns (e.g., kingdom, phylum, class, order, family, genus). The species column is used for matching and is excluded from the enrichment analysis. SummarizedExperiment input: Taxonomy is extracted from rowData() and feature identifiers from rownames(). If the mia package is installed, taxonomyRanks() is used to identify taxonomic rank columns; otherwise all rowData() columns are used. The Species rank column is automatically excluded from the analysis. Requires the SummarizedExperiment package.
min_set_size	Minimum number of species in a set to include in the analysis. Default is 5.
max_set_size	Maximum number of species in a set to include in the analysis. Default is 100.

Value

A named list of data frames, one per taxonomic rank. Each data frame contains columns: taxon-SetName, median_rank_of_set_members, PValue, Test_statistic, and FDR. Ranks that produce no valid sets (e.g., due to size filtering) are included as empty data frames with a message.

Examples

```
# --- Example 1: Data frame input ---
# Create a lineage data frame (e.g., parsed from curatedMetagenomicData)
# The 'species' column must match the names in taxon_ranks.

lineage_df <- data.frame(
  species = c("Cutibacterium_acnes", "Klebsiella_pneumoniae",
    "Propionibacterium_humerusii", "Moraxella_osloensis",
    "Enhydrobacter_aerosaccus", "Staphylococcus_capitis",
    "Staphylococcus_epidermidis", "Staphylococcus_aureus",
```

```

      "Escherichia_coli", "Enterobacter_cloacae",
      "Pseudomonas_aeruginosa", "Acinetobacter_baumannii",
      "Lactobacillus_rhamnosus", "Lactobacillus_acidophilus",
      "Bifidobacterium_longum", "Bifidobacterium_breve"),
kingdom = rep("Bacteria", 16),
phylum = c("Actinobacteria", "Proteobacteria",
             "Actinobacteria", "Proteobacteria",
             "Proteobacteria", "Firmicutes",
             "Firmicutes", "Firmicutes",
             "Proteobacteria", "Proteobacteria",
             "Proteobacteria", "Proteobacteria",
             "Firmicutes", "Firmicutes",
             "Actinobacteria", "Actinobacteria"),
class = c("Actinobacteria", "Gammaproteobacteria",
          "Actinobacteria", "Gammaproteobacteria",
          "Alphaproteobacteria", "Bacilli",
          "Bacilli", "Bacilli",
          "Gammaproteobacteria", "Gammaproteobacteria",
          "Gammaproteobacteria", "Gammaproteobacteria",
          "Bacilli", "Bacilli",
          "Actinobacteria", "Actinobacteria"),
order = c("Propionibacteriales", "Enterobacterales",
          "Propionibacteriales", "Pseudomonadales",
          "Rhodospirillales", "Bacillales",
          "Bacillales", "Bacillales",
          "Enterobacterales", "Enterobacterales",
          "Pseudomonadales", "Pseudomonadales",
          "Lactobacillales", "Lactobacillales",
          "Bifidobacteriales", "Bifidobacteriales"),
family = c("Propionibacteriaceae", "Enterobacteriaceae",
          "Propionibacteriaceae", "Moraxellaceae",
          "Rhodospirillaceae", "Staphylococcaceae",
          "Staphylococcaceae", "Staphylococcaceae",
          "Enterobacteriaceae", "Enterobacteriaceae",
          "Pseudomonadaceae", "Moraxellaceae",
          "Lactobacillaceae", "Lactobacillaceae",
          "Bifidobacteriaceae", "Bifidobacteriaceae"),
genus = c("Cutibacterium", "Klebsiella",
          "Cutibacterium", "Moraxella",
          "Enhydrobacter", "Staphylococcus",
          "Staphylococcus", "Staphylococcus",
          "Escherichia", "Enterobacter",
          "Pseudomonas", "Acinetobacter",
          "Lactobacillus", "Lactobacillus",
          "Bifidobacterium", "Bifidobacterium"),
stringsAsFactors = FALSE
)

set.seed(42)
fc <- setNames(rnorm(16), lineage_df$species)
results <- taxon_rank_sets(fc, lineage_df, min_set_size = 2)
names(results)
results$family

```

```
# --- Example 2: SummarizedExperiment / TreeSummarizedExperiment input ---
## Not run:
library(mia)
data(GlobalPatterns, package = "mia")
tse <- GlobalPatterns

# Run differential abundance (e.g., ALDEx2) to get fold changes
# aldex_out <- ... (your DA analysis)
# fc <- aldex_out$effect
# names(fc) <- rownames(aldex_out)

# Run taxon rank set enrichment directly from the TSE
results <- taxon_rank_sets(fc, tse, min_set_size = 5)
names(results) # Kingdom, Phylum, Class, Order, Family, Genus
results$Family

## End(Not run)
```

TaxSEA

TaxSEA: Taxon Set Enrichment Analysis

Description

Modular TaxSEA implementation supporting enrichment (KS) and ORA (Fisher). Provide either `taxon_ranks` for enrichment or `input_taxa` for ORA.

Usage

```
TaxSEA(
  taxon_ranks = NULL,
  input_taxa = NULL,
  mode = NULL,
  lookup_missing = FALSE,
  min_set_size = 5,
  max_set_size = 300,
  custom_db = NULL
)
```

Arguments

<code>taxon_ranks</code>	Named numeric vector of statistics (e.g., log2 fold changes). Required for enrichment.
<code>input_taxa</code>	Character vector of taxa to treat as "hits"/selected taxa. Required for ORA.
<code>mode</code>	Character. One of "enrichment" or "ora". If NULL, inferred from which input is provided.
<code>lookup_missing</code>	Logical indicating whether to fetch missing NCBI IDs. Default is FALSE.

min_set_size	Minimum size of taxon sets to include in the analysis. Default is 5.
max_set_size	Maximum size of taxon sets to include in the analysis. Default is 100.
custom_db	A user-provided list of taxon sets. If NULL (default), the built-in database is used.

Value

A list of data frames with taxon set results.

Examples

```
data("TaxSEA_test_data")
res <- TaxSEA(taxon_ranks = TaxSEA_test_data)
head(res$All_databases)

# ORA example (toy): treat taxa with positive values as "hits"
hits <- names(TaxSEA_test_data)
res_ora <- TaxSEA(input_taxa = hits, mode = "ora")
head(res_ora$All_databases)
```

TaxSEA_db	<i>TaxSEA Database A dataset containing taxon sets. Each item in the list is a taxon set, and each member within a taxon set is a taxon.</i>
-----------	--

Description

TaxSEA Database A dataset containing taxon sets. Each item in the list is a taxon set, and each member within a taxon set is a taxon.

Usage

TaxSEA_db

Format

A list of vectors. Each vector contains character strings representing taxa.

Source

See READ ME.

Examples

```
data(TaxSEA_db)
all_sets <- names(TaxSEA_db)
GABA_producers<-TaxSEA_db[["MiMeDB_producers_of_GABA"]]
```

TaxSEA_test_data	<i>TaxSEA Test Data</i>
------------------	-------------------------

Description

A dataset containing taxon ranks and taxon IDs.

Usage

```
TaxSEA_test_data
```

Format

A data frame with two columns:

rank Character vector representing taxon ranks

id Character vector representing taxon IDs

A data frame with columns 'rank' and 'id' representing taxon ranks and taxon IDs, respectively.

Source

See READ ME.

Examples

```
data(TaxSEA_test_data)
test_results <- TaxSEA(TaxSEA_test_data)
```

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