Package 'RFGeneRank'

April 24, 2026

Title RFGeneRank: Cross-validated Stable Predictive Gene Ranking for Transcriptomics

Version 0.99.4

Description Tools to harmonize bulk RNA-seq matrices, optionally apply batch correction, and train cross-validated classification models using ranger, glmnet, or xgboost. Supports leakage-safe feature selection, permutation importance, SHAP-based interpretability, and calibration methods (Platt or isotonic). Provides stability metrics across folds, embeddings (PCA/UMAP), ROC visualization, SHAP dependence plots, and tidy ranked-gene tables for downstream analysis.

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URL https://github.com/Abdulaziz-Albeshri/RFGeneRank

BugReports https://github.com/Abdulaziz-Albeshri/RFGeneRank/issues

Depends R (>= 4.6.0)

Imports ggplot2, limma, methods, pROC, ranger, stats, SummarizedExperiment, sva, AnnotationDbi, umap, scales, utils, S4Vectors, digest, mgcv, Matrix, glmnet, xgboost, patchwork

Suggests GEOquery, Biobase, edgeR, uwot, BiocStyle, knitr, org.Hs.eg.db, rmarkdown, DESeq2, MASS, matrixStats, BiocGenerics, fastshap, caret, testthat (>= 3.0.0), covr

Config/testthat/edition 3

VignetteBuilder knitr

biocViews Transcriptomics, RNASeq, GeneExpression, FeatureExtraction, Classification, Visualization, Software, StatisticalMethod, Alignment

Encoding UTF-8

Roxygen list(markdown = TRUE)

RoxygenNote 7.3.3

Collate 'globals.R' 'class_def.R' 'accessors.R' 'accessors_public.R' 'check_utils.R' 'batch_correct.R' 'calibrate.R' 'combat_helpers.R' 'compute_class_weights.R' 'confounding.R' 'crossval.R' 'id_map.R' 'plots_all.R' 'prepare_data.R'

'align_datasets.R' 'rank_genes.R' 'top_genes.R' 'Rzzz.R'
'package-doc.R' 'sign_importance.R' 'factor_dependence.R'
'validate_genes.R'

NeedsCompilation no

git_url https://git.bioconductor.org/packages/RFGeneRank

git_branch devel

git_last_commit 7bc34fc

git_last_commit_date 2026-04-06

Repository Bioconductor 3.23

Date/Publication 2026-04-23

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`align_datasets` *Align and merge expression + metadata (genes by intersection; strict sample match)*

Description

`align_datasets()` ingests parallel lists of expression tables (matrices/data.frames) and metadata data.frames, cleans them, enforces strict sample alignment (`rownames(metadata)` == `colnames(expression)`), drops metadata rows with any NA (with a warning + structured report), merges by the intersection of genes, and returns the merged expression, metadata, and a `SummarizedExperiment` with gene IDs locked into `rowData(se)$gene_id`.

No regex recoding is performed. If a dataset lacks a `batch` column and `require_batch=TRUE`, a per-dataset batch factor ("Batch1", "Batch2", ...) is created.

Usage

```
align_datasets(
  expr_list,
  meta_list,
  prefer = NULL,
  require_batch = TRUE,
  tag_dataset = TRUE,
  gene_merge = "intersection",
  verbose = TRUE
)
```

Arguments

`expr_list` list of matrices or data.frames; rows = genes, cols = samples. If a data.frame contains a gene-ID column, it will be moved into rownames. All expression values are coerced to numeric (double).

`meta_list` list of data.frames; rows = samples (must be in rownames). Must contain a `state` column and (if `require_batch=TRUE`) a `batch` column. If `batch` is missing, it is auto-created per dataset as "Batch1", "Batch2", etc.

`prefer` optional selector/renamer for metadata columns. Two forms are supported:

- index form: c("2:state","5:batch") (select column 2 and 5, rename to state,batch)
- name map: c("state=phenotype","batch=plate") (select phenotype, rename to state, etc.) Accepts either a single character vector applied to all datasets, or a named list specifying datasets individually. with one vector per dataset (names must match names(expr_list)/names(meta_list)). No value recoding is performed.

`require_batch` logical (default TRUE). If TRUE and a dataset lacks `batch`, create a per-dataset batch factor ("Batch1", "Batch2", etc.).

`tag_dataset` logical (default TRUE). If TRUE, add a `dataset` factor ("ds1","ds2",...) to the merged metadata.

`gene_merge`	character(1), default "intersection". Currently only intersection is supported (keeps only genes shared by all datasets).
`verbose`	logical. If TRUE (default), prints a brief summary and per-dataset stats.

Value

A list with:

expr Merged numeric matrix (genes x samples) with syntactic, unique gene IDs.

metadata Merged metadata (samples as rownames) with `state`/`batch` as factors.

se A `SummarizedExperiment` with assay "expr", `colData` = `metadata`, and `rowData(se)$gene_id` set to current rownames.

report List with per-dataset input/kept counts, NA-drop details, observed levels, and final shared-gene count.

Align and merge expression + metadata ...

Examples

```
# Single toy dataset: expression matrix (genes x samples)
expr <- matrix(
  rnorm(5 * 4),
  nrow = 5,
  dimnames = list(
    paste0("gene", 1:5),
    paste0("s1_", 1:4)
  )
)

# Matching metadata: one row per sample, with 'state' and 'batch' columns
meta <- data.frame(
  state = rep("Control", ncol(expr)),
  batch = rep("A",       ncol(expr))
)
rownames(meta) <- colnames(expr)

# Lists of length 1 for expression and metadata
expr_list <- list(A = expr)
meta_list <- list(A = meta)

aligned <- align_datasets(
  expr_list = expr_list,
  meta_list = meta_list
)
str(aligned)
```

apply_calibration — *Apply stored calibration to a numeric vector of probabilities*

Description

Apply stored calibration to a numeric vector of probabilities

Usage

```
apply_calibration(fit, p)
```

Arguments

`fit`	GeneRankFit with stored calibration information.
`p`	numeric vector of positive-class probabilities

Value

numeric vector of calibrated probabilities (or original if none stored)

Examples

```
# Example probabilities
p <- runif(5)

# Minimal GeneRankFit without calibration (returns original p)
fit0 <- methods::new("GeneRankFit")
apply_calibration(fit0, p)
```

calibrate_oof — *Calibrate out-of-fold probabilities (isotonic or Platt)*

Description

Fits a calibration model on the out-of-fold (OOF) positive-class probabilities and stores it inside the GeneRankFit object. No data leakage: uses OOF only.

Usage

```
calibrate_oof(fit, method = c("isotonic", "platt"))
```

Arguments

`fit`	GeneRankFit containing out-of-fold predictions and labels.
`method`	"isotonic" or "platt"

Value

GeneRankFit with stored calibration information.

Examples

```
# Example probabilities
p <- runif(5)

# Case 1: no calibration stored → returns original p
fit0 <- methods::new("GeneRankFit")
apply_calibration(fit0, p)

# Case 2: simple calibration function (illustration)
fit1 <- methods::new("GeneRankFit")
calibration(fit1) <- list(fun = function(x) x^0.8)
apply_calibration(fit1, p)
```

---

factor_dependence *Covariate dependence of gene contributions (SHAP/proxy; "expr" assay)*

Description

Covariate dependence of gene contributions (SHAP/proxy; "expr" assay)

Usage

```
factor_dependence(
  fit,
  se,
  covariates,
  method = c("shap", "proxy"),
  ngenes = 500L,
  gene_selection = c("importance", "variance"),
  nsim = 128L,
  bg_per_class = 64L,
  cache_dir = NULL,
  fdr_method = "BH",
  seed = 1L,
  pred_fun = NULL,
  pos_label = NULL,
  positive = NULL
)
```

Arguments

`fit`	Trained object containing out-of-fold predictions (n x k) and labels. For S4 wrappers (e.g., GeneRankFit), the finalized learner should be in A final fitted model and the training feature names may also be present. this function will train a temporary full-data model on-the-fly (not saved).
`se`	SummarizedExperiment with assay "expr" (genes x samples).
`covariates`	Character vector of covariate names in colData(se), e.g. c("sex","age").
`method`	"shap" (default; uses fastshap if available) or "proxy".
`ngenes`	Number of genes to test (default 500). Use "ALL" or NULL for all genes.
`gene_selection`	"importance" (default) or "variance".
`nsim`	SHAP Monte-Carlo permutations (default 128).
`bg_per_class`	Max background samples per class for SHAP (default 64).
`cache_dir`	Cache directory for SHAP matrices; default R user cache dir.
`fdr_method`	Multiple-testing correction (default "BH").
`seed`	RNG seed (default 1).
`pred_fun`	OPTIONAL user predictor: function(newdata) -> numeric p(positive). If provided, it takes precedence over the built-in predictor.
`pos_label`	OPTIONAL (legacy) positive class label; kept for back-compat.
`positive`	OPTIONAL override for positive class. Either a class label (character) or an index 1/2. If provided, it overrides `pos_label`.

Value

data.frame with columns: gene, covariate, test, stat, pval, fdr, effect, dependent. Attributes: "method","assay","genes_used","

Examples

```
#' # For reproducibility, set a fixed seed such as set.seed(1) before running this example.

# Tiny expression matrix
expr <- matrix(stats::rnorm(30), nrow = 6)
rownames(expr) <- paste0("gene", 1:6)
colnames(expr) <- paste0("sample", 1:5)

# Covariates
cd <- data.frame(
  label = factor(c("A", "A", "B", "B", "B")),
  sex   = factor(c("M", "F", "F", "M", "M")),
  age   = c(30, 40, 35, 50, 60)
)

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = cd
)
```

```
# Minimal mock GeneRankFit object with required slots
prob_mat <- matrix(
  stats::runif(5),
  ncol = 1,
  dimnames = list(colnames(se), "B")
)

fit <- methods::new(
  "GeneRankFit",
  oof = list(
    prob = prob_mat,
    y    = cd$label
  )
)
```

GeneRankFit-accessors *Accessors for GeneRankFit*

Description

Getter/setter accessors for GeneRankFit slots.

Usage

```
params(x)

## S4 method for signature 'GeneRankFit'
params(x)

oof(x)

## S4 method for signature 'GeneRankFit'
oof(x)

imp(x)

## S4 method for signature 'GeneRankFit'
imp(x)

imp(x) <- value

## S4 replacement method for signature 'GeneRankFit'
imp(x) <- value

calibration(x)

## S4 method for signature 'GeneRankFit'
```

```
calibration(x)

calibration(x) <- value

## S4 replacement method for signature 'GeneRankFit'
calibration(x) <- value
```

Arguments

`x`	A `GeneRankFit` object.
`value`	Replacement value.

Value

For getters:

`params(x)` A list of training parameters and metadata.

`oof(x)` A list of out-of-fold results including predictions and labels.

`imp(x)` A `data.frame` containing aggregated variable importance scores.

`calibration(x)` A list describing calibration settings.

For setters:

`imp(x) <- value` Returns the updated `GeneRankFit` object with modified importance data.

`calibration(x) <- value` Returns the updated `GeneRankFit` object with modified calibration settings.

Examples

```
fit <- methods::new("GeneRankFit")

# getters
params(fit)
oof(fit)
imp(fit)
calibration(fit)

# setters
imp(fit) <- data.frame(
  gene = c("GeneA", "GeneB"),
  importance = c(0.8, 0.3)
)
calibration(fit) <- list(
  method = "platt",
  fun = function(p) p
)

imp(fit)
calibration(fit)
```

id_map — *Map gene identifiers using AnnotationDbi*

Description

A thin wrapper around `AnnotationDbi::select()` that preserves input preserves order and enables straightforward conversion between identifier types (e.g., ENTREZID $\rightarrow$ SYMBOL).

Usage

```
id_map(
  keys,
  from,
  to,
  OrgDb = org.Hs.eg.db::org.Hs.eg.db,
  drop_na = TRUE,
  unique = TRUE
)
```

Arguments

`keys`	character vector of gene IDs to map (e.g., ENTREZ IDs).
`from`	source keytype (e.g., "ENTREZID", "ENSEMBL", "SYMBOL").
`to`	destination keytype (e.g., "SYMBOL").
`OrgDb`	an `OrgDb` object. Defaults to `org.Hs.eg.db`.
`drop_na`	logical; if TRUE, drop rows with missing mapped values.
`unique`	logical; if TRUE, keep at most one mapping per input key, preferring the first match returned by `AnnotationDbi::select()`.

Value

data.frame with columns `from`, `to` in that order.

Examples

```
if (requireNamespace("org.Hs.eg.db", quietly = TRUE)) {
  x <- c("7157", "7158")  # ENTREZ IDs
  id_map(x, from = "ENTREZID", to = "SYMBOL")
}
```

plot_confusion_heatmap — *Confusion-matrix heatmap*

Description

Confusion-matrix heatmap

Usage

```
plot_confusion_heatmap(cm, mode = c("counts", "rowpct"))
```

Arguments

`cm`	A 2x2 table as returned by `val$<method>$conf_mat`.
`mode`	Either `"counts"` or `"rowpct"`.

Value

A ggplot object.

Examples

```
# For reproducibility, specify a fixed seed (e.g., set.seed(1)) before running this example.

true <- factor(rep(c("A", "B"), each = 5))
pred <- factor(sample(c("A", "B"), 10, replace = TRUE))

tab <- table(True = true, Predicted = pred)

plot_confusion_heatmap(tab)
```

plot_embed — *Decision-space embedding (OOF probability space): PCA or UMAP*

Description

Embeds samples using the out-of-fold (OOF) probability space (2D). Good for inspecting decision geometry; for biology structure, prefer `plot_embed_expr()`.

Usage

```
plot_embed(
  fit,
  type = c("pca", "umap"),
  engine = c("umap", "uwot"),
  neighbors = NULL,
  min_dist = NULL,
  metric = NULL,
  seed = NULL,
  point_size = 2,
  show_legend = TRUE,
  palette = NULL
)
```

Arguments

`fit`	GeneRankFit (must have OOF probabilities).
`type`	`"pca"` or `"umap"`.
`engine`	UMAP engine if type="umap" (`"umap"` or `"uwot"`).
`neighbors`, `min_dist`, `metric`, `seed`	UMAP params.
`point_size`	numeric
`show_legend`	logical
`palette`	optional manual color palette

Value

A ggplot object.

Examples

```
# For reproducibility, specify a fixed seed (e.g., set.seed(1)) before running this example.

# Toy 2D embedding for 10 samples
embed_df <- data.frame(
  sample = paste0("sample", 1:10),
  dim1   = rnorm(10),
  dim2   = rnorm(10),
  label  = factor(rep(c("A", "B"), each = 5))
)

head(embed_df)
```

plot_embed_expr *Expression-space embedding (PCA or UMAP) of top RF genes*

Description

Plots samples in the original expression space using the top RF-ranked genes. For PCA, axis labels include the percent variance explained. For UMAP, the title shows the engine and key parameters used.

Usage

```
plot_embed_expr(
  fit,
  se,
  n_top = 100,
  type = c("umap", "pca"),
  engine = c("umap", "uwot"),
  neighbors = 15,
  min_dist = 0.1,
  metric = "euclidean",
  zscore = TRUE,
  seed = NULL,
  point_size = 2,
  show_legend = TRUE,
  palette = NULL
)
```

Arguments

fit	GeneRankFit
se	SummarizedExperiment with assay "expr"
n_top	integer; number of top RF genes to use (default 100)
type	"umap" or "pca"
engine	UMAP engine, "umap" or "uwot" (used when type="umap")
neighbors, min_dist, metric	UMAP parameters
zscore	Logical; z-score samples x genes matrix before embedding (default TRUE)
seed	RNG seed for UMAP reproducibility (default uses stored pipeline seed if available).
point_size	numeric
show_legend	logical
palette	optional named vector of colors (names must match levels)

Value

A ggplot object.

Examples

```
# For reproducibility, specify a fixed seed (e.g., set.seed(1)) before running this example.

# Toy expression: 15 genes × 8 samples
expr <- matrix(rnorm(15 * 8), nrow = 15)
rownames(expr) <- paste0("gene", 1:15)
colnames(expr) <- paste0("sample", 1:8)

# Binary labels for samples
label <- factor(rep(c("A", "B"), each = 4))

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = data.frame(label = label)
)

se
```

---

plot_importance *Feature importance (top genes)*

Description

Uses fold-normalized mean importances aggregated across CV folds. To display gene SYMBOLs on the axes, set `map_to_symbol = TRUE`. (requires org.Hs.eg.db and RFGeneRank::top_genes()).

Usage

```
plot_importance(
  fit,
  top = 30,
  map_to_symbol = FALSE,
  from = "ENTREZID",
  to = "SYMBOL"
)
```

Arguments

`fit`	GeneRankFit from `rank_genes()`.
`top`	Integer; number of genes to display (default 30).
`map_to_symbol`	Logical; map gene IDs to symbols if available (default FALSE).
`from`	Keytype for input IDs (default "ENTREZID").
`to`	Keytype for output labels (default "SYMBOL").

Value

A ggplot object.

Examples

```
# Toy expression matrix: genes x samples
expr <- matrix(
  rnorm(10 * 20),
  nrow = 10,
  dimnames = list(
    paste0("gene", 1:10),
    paste0("sample", 1:20)
  )
)

# Binary phenotype stored in 'label' column
y <- factor(rep(c("Control", "Case"), each = 10))

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = data.frame(
    label    = y,
    row.names = colnames(expr)
  )
)

# Fit a small GeneRank model (note: no 'genes' argument)
fit <- rank_genes(
  se        = se,
  label_col = "label",
  n_top     = 10,
  trees     = 200
)

# Plot feature importance for the top-ranked genes
plot_importance(fit)
```

---

plot_roc *ROC curve from OOF probabilities (single model)*

Description

ROC curve from OOF probabilities (single model)

Usage

```
plot_roc(fit)
```

Arguments

fit GeneRankFit with stored out-of-fold predictions and labels.

Value

A ggplot2 object containing the ROC curve derived from

Examples

```
expr <- matrix(
  rnorm(10 * 20),
  nrow = 10,
  dimnames = list(
    paste0("gene", 1:10),
    paste0("sample", 1:20)
  )
)

y <- factor(rep(c("Control", "Case"), each = 10))

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = data.frame(state = y)
)

fit <- rank_genes(se, label_col = "state", trees = 100)
plot_roc(fit)
```

---

plot_roc_multi *Multi-model ROC (guardrailed OOF)*

Description

Overlays ROC curves for one or more fits that expose `$oof` with `p_use` and `y`. Works with `validate_genes()` outputs.

Usage

```
plot_roc_multi(fits, title = "ROC (OOF, guardrailed)")
```

Arguments

fits Named list of model results (e.g., `list(ranger=val$ranger, ...)`).

title Character plot title.

Value

A ggplot object.

Examples

```
# Toy binary outcome
y <- factor(rep(c("Control", "Case"), each = 10))

# Positive-class probabilities (Case = positive class)
p_use1 <- runif(20)
p_use2 <- runif(20)

# Create minimal fit objects expected by plot_roc_multi()
fits <- list(
  Model_1 = list(
    oof = list(
      y = y,
      p_use = p_use1
    )
  ),
  Model_2 = list(
    oof = list(
      y = y,
      p_use = p_use2
    )
  )
)

plot_roc_multi(fits)
```

`plot_shap_dependence` *SHAP dependence scatter for one gene (cached-first, robust, fast)*

Description

SHAP dependence scatter for one gene (cached-first, robust, fast)

Usage

```
plot_shap_dependence(
  fit,
  se,
  gene,
  x = "age",
  color_by = NULL,
  palette = NULL,
  shap_mat = NULL,
  nsim = 64,
  pos_label = NULL,
  age_band_width = 10,
  band_alpha = 0.12,
  band_mode = c("significant", "top_k"),
  top_k = 1
)
```

Arguments

- `fit` GeneRankFit containing out-of-fold predictions and labels.
- `se` SummarizedExperiment with assay "expr".
- `gene` Character gene ID present in assay(se,"expr").
- `x` Covariate name in colData(se) for x-axis (default "age").
- `color_by` Optional grouping column name in colData(se); if NULL, no colour grouping.
- `palette` Optional character vector of colour names or hex codes. If `color_by` is:
  - numeric: `palette` (length >= 2) is used as a continuous gradient via `scale_color_gradientn()`.
  - categorical: `palette` is recycled/trimmed to the number of levels and used via `scale_color_manual()`.

  If `palette` is NULL, ggplot2 defaults are used, except for `color_by = "sex"` / `"sex_clean"` where a fixed pink/cyan palette is used.
- `shap_mat` Optional SHAP matrix (rows = samples, cols = genes).
- `nsim` Fastshap nsim if auto-computing (default 64).
- `pos_label` Positive class label (defaults to level 2 of outcome).
- `age_band_width` Width of shaded age bands (years) for sex plots.
- `band_alpha` Alpha of bands.
- `band_mode` "significant" (FDR<=0.05) or "top_k".
- `top_k` If band_mode="top_k", how many bins per group to shade.

Value

ggplot object.

Examples

```
expr <- matrix(
  rnorm(10 * 20),
  nrow = 10,
  dimnames = list(
    paste0("gene", 1:10),
    paste0("sample", 1:20)
  )
)

y <- factor(rep(c("Control", "Case"), each = 10))

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = data.frame(
    state = y,
    age   = seq_len(20) + 40
  )
)
```

```
fit <- rank_genes(se, label_col = "state", trees = 50)

# Minimal SHAP-like matrix: one column named by the gene
shap_mat <- matrix(
  rnorm(20),
  nrow = 20,
  dimnames = list(NULL, "gene1")
)

plot_shap_dependence(
  fit      = fit,
  se       = se,
  gene     = "gene1",
  x        = "age",
  shap_mat = shap_mat
)
```

---

plot_sign_importance *Signed feature importance (directional effect)*

Description

Visualizes direction-aware importances produced by `sign_importance()`. If `tab` is NULL, the function will try to read the stored importance table and require a `signed_importance` column to be present there.

Usage

```
plot_sign_importance(
  fit = NULL,
  tab = NULL,
  top = 30,
  map_to_symbol = FALSE,
  from = "ENTREZID",
  to = "SYMBOL",
  show_legend = TRUE,
  palette = NULL
)
```

Arguments

`fit`	GeneRankFit (optional if `tab` is supplied)
`tab`	data.frame from `sign_importance()` with columns: gene, importance, direction (-1/0/1), signed_importance
`top`	Integer; number of genes to show (default 30)
`map_to_symbol`	Logical; map x-axis labels to SYMBOLs (default FALSE)
`from`	Keytype for input IDs (default "ENTREZID")

to	Keytype for output labels (default "SYMBOL")
show_legend	Logical; show legend (default TRUE)
palette	Optional named vector for fill colors, e.g. `` c(`-1`="#3182bd", `1`="#de2d26", `0`="#9e9e9e") ``

Value

A ggplot object.

Examples

```
# Toy signed importance table for 5 genes
signed_imp <- data.frame(
  gene        = paste0("gene", 1:5),
  importance  = c(0.5, 0.4, 0.3, 0.2, 0.1),
  signed_effect = c(0.5, -0.4, 0.3, -0.2, 0.1)
)

head(signed_imp)
```

---

prepare_data *Prepare matrices + metadata: align, (log) transform, batch correct, prefilter*

Description

Prepare matrices + metadata: align, (log) transform, batch correct, prefilter

Usage

```
prepare_data(
  mats,
  metas,
  label_col,
  batch_col = NULL,
  n_var = 5000,
  log1p = TRUE,
  batch_method = c("none", "combat", "limma", "combat_seq"),
  counts = FALSE,
  filter_in_cv = FALSE,
  batch_correction_scope = c("global", "fold"),
  batch_covariates = NULL
)
```

Arguments

`mats`	list of numeric matrices (genes-by-samples)
`metas`	list of data.frames (rownames = sample IDs)
`label_col`	outcome column in metadata
`batch_col`	batch column in metadata (or NULL)
`n_var`	keep top-N variable genes globally (unsupervised)
`log1p`	logical; log1p transform before variance filter
`batch_method`	"none","combat","limma","combat_seq"
`counts`	logical; TRUE if raw counts (for combat_seq)
`filter_in_cv`	logical; if TRUE, skip global variance filter and let CV do it inside folds
`batch_correction_scope`	"global" or "fold" (fold correction happens inside CV)
`batch_covariates`	optional character vector of metadata column names used as covariates in batch correction

Value

SummarizedExperiment

Examples

```
set.seed(1)

expr <- matrix(stats::rnorm(20 * 10), nrow = 20)
rownames(expr) <- paste0("gene", 1:20)
colnames(expr) <- paste0("sample", 1:10)

label  <- factor(rep(c("A", "B"), each = 5))
batch  <- factor(rep(c("batch1", "batch2"), times = 5))

# Build lists of matrices + metadata as expected by prepare_data()
mats  <- list(expr)
metas <- list(data.frame(
  label = label,
  batch = batch,
  row.names = colnames(expr)
))

prep <- prepare_data(
  mats      = mats,
  metas     = metas,
  label_col = "label",
  batch_col = "batch"
)
prep
```

rank_genes *Rank genes with batch-aware cross-validation (UMAP-free)*

Description

Performs CV on a SummarizedExperiment, aggregates fold-normalized feature importances, and stores out-of-fold predictions. Supports K-fold, LOBO (Leave-One-Batch-Out), and group-K by batch. Batch correction, filtering, transforms, and standardization are applied *inside folds* using TRAIN-only statistics. If `auto_confounds=TRUE`, the function inspects batch~label association and will switch to LOBO and enable fold-safe batch correction if confounding is moderate/severe.

Usage

```
rank_genes(
  se,
  label_col = "state",
  n_top = 500,
  k = 5,
  trees = 1000,
  importance = c("permutation", "impurity"),
  class_weights = NULL,
  threads = max(1, parallel::detectCores() - 1),
  seed = 1,
  fold_batch_correction = FALSE,
  batch_col = NULL,
  batch_covariates = NULL,
  filter_low_expr = FALSE,
  min_prop = 0.2,
  transform = c("none", "log1p"),
  standardize = FALSE,
  cv = c("kfold", "lobo", "groupk"),
  auto_confounds = TRUE
)
```

Arguments

`se`	SummarizedExperiment
`label_col`	character; class-label column in colData(se)
`n_top`	integer; per-fold top-variance feature count (0 = off)
`k`	integer; number of folds (ignored by LOBO)
`trees`	integer; number of trees for ranger
`importance`	"permutation" or "impurity"
`class_weights`	named numeric vector or NULL (auto-computed if NULL and imbalance >= 1.5x)
`threads`	integer; CPU threads for ranger

`seed` integer; RNG seed

`fold_batch_correction`
: logical; if TRUE, do train-only batch removal per fold

`batch_col` optional; name of batch column in colData(se)

`batch_covariates`
: optional character vector of covariates for batch model

`filter_low_expr`
: logical; drop genes expressed (>0) in < min_prop of TRAIN

`min_prop` numeric in (0,1]; minimum TRAIN proportion to keep a gene

`transform` "none" or "log1p"

`standardize` logical; z-score by TRAIN mean/SD (applied to train+test)

`cv` "kfold", "lobo", or "groupk"

`auto_confounds` logical; if TRUE, auto-switch to LOBO and enable fold batch-correction when confounded

Value

GeneRankFit S4 object

Examples

```
# For reproducibility, specify a fixed seed (e.g., set.seed(1)) before running this example.

# Toy expression: 20 genes × 12 samples
expr <- matrix(stats::rnorm(20 * 12), nrow = 20)
rownames(expr) <- paste0("gene", 1:20)
colnames(expr) <- paste0("sample", 1:12)

# Binary labels
label <- factor(rep(c("A", "B"), each = 6))

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = data.frame(label = label)
)

# Rank genes with default settings
rg <- rank_genes(
  se        = se,
  label_col = "label"
)

str(rg)
```

RFGeneRank *RFGeneRank: CV-stable predictive ranking for transcriptomics*

Description

Package-level documentation and imports.

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See Also

Useful links:

- https://github.com/Abdulaziz-Albeshri/RFGeneRank
- Report bugs at https://github.com/Abdulaziz-Albeshri/RFGeneRank/issues

---

rfgr_crossval *Batch-aware cross-validation with optional ComBat modes (incl. frozen ComBat)*

Description

Orchestrates leakage-safe CV for RFGeneRank with two ComBat modes:

- "none": no batch correction
- "train": train-only batch correction with leakage-safe application to TEST

Supports LOBO (leave-one-batch-out), Group K-Fold by batch, and standard K-Fold.

Usage

```
rfgr_crossval(
  expr,
  metadata,
  label_col = "state",
  batch_col = "batch",
  covariates = NULL,
  cv = c("lobo", "groupk", "kfold"),
  k = 5,
  combat_mode = c("none", "train"),
  rf_trees = 1000,
  seed = 1,
  verbose = TRUE
)
```

Arguments

`expr`	numeric matrix genes x samples (continuous scale: log2CPM or log2(TPM+1))
`metadata`	data.frame with SampleID, label_col, batch_col
`label_col`	character; target column in metadata (e.g., "state")
`batch_col`	character; batch/dataset column in metadata (e.g., "batch")
`covariates`	character vector of column names to *preserve* in ComBat (added to design)
`cv`	one of c("lobo","groupk","kfold")
`k`	integer; number of folds for "groupk" or "kfold"
`combat_mode`	one of c("none","train")
`rf_trees`	integer; number of trees for ranger
`seed`	integer; RNG seed
`verbose`	logical; emit progress messages

Value

list(auc_by_fold, mean_auc, settings, folds_info)

Examples

```
# Minimal runnable example: tiny dataset, fast evaluation
expr <- matrix(rnorm(10 * 6), nrow = 10)
rownames(expr) <- paste0("gene", 1:10)
colnames(expr) <- paste0("sample", 1:6)

label <- factor(rep(c("A", "B"), each = 3))
batch <- factor(rep(c("batch1", "batch2"), times = 3))

metadata <- data.frame(
  label = label,
  batch = batch,
```

```
  row.names = colnames(expr)
)

# Lightweight cross-validation: no ComBat, few trees
cv_res <- rfgr_crossval(
  expr        = expr,
  metadata    = metadata,
  label_col   = "label",
  batch_col   = "batch",
  cv          = "kfold",
  k           = 2,
  combat_mode = "none",
  rf_trees    = 10,
  verbose     = FALSE
)

cv_res
```

`rfgr_plot_suite` *One-call plot suite (optional file export)*

Description

Produces: importance, signed-importance, expression PCA, decision PCA, ROC overlay (if `val` provided), confusion heatmaps, and optional SHAP.

Usage

```
rfgr_plot_suite(fit, se, val = NULL, outdir = NULL, top = 30, shap_gene = NULL)
```

Arguments

`fit`	GeneRankFit from `rank_genes()`.
`se`	SummarizedExperiment with assay "expr".
`val`	Optional result from `validate_genes()`.
`outdir`	Optional directory to save PNGs (if not NULL).
`top`	Integer; number of genes in importance plots.
`shap_gene`	Optional gene ID for SHAP dependence.

Value

(Invisibly) list of ggplot objects.

Examples

```
# Toy expression matrix: genes x samples
expr <- matrix(
  rnorm(10 * 12),
  nrow = 10
)

# Use known human Entrez IDs as gene names so annotation works
rownames(expr) <- c(
  "1",    # A1BG
  "2",    # A2M
  "9",    # NAT1
  "1956", # EGFR
  "2064", # ERBB2
  "5290", # PIK3CA
  "5728", # PTEN
  "7422", # VEGFA
  "1950", # EDN1
  "7157"  # TP53
)

colnames(expr) <- paste0("sample", 1:12)

# Binary phenotype stored in 'label' column
label <- factor(rep(c("Control", "Case"), each = 6))

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = data.frame(
    label     = label,
    row.names = colnames(expr)
  )
)

# Fit a small GeneRank model
fit <- rank_genes(
  se        = se,
  label_col = "label",
  n_top     = 10,
  trees     = 100
)

# For this example, ensure the stored importance table has signed_importance information
# required by plot_sign_importance().
imp0 <- imp(fit)
if (is.null(imp0)) {
  imp0 <- data.frame(
    gene = character(),
    importance = numeric(),
    direction = integer(),
    signed_importance = numeric(),
    stringsAsFactors = FALSE
```

```
  )
}
if (!"direction" %in% colnames(imp0)) {
  imp0$direction <- 1L
}
if (!"signed_importance" %in% colnames(imp0)) {
  imp0$signed_importance <- imp0$importance * imp0$direction
}
imp(fit) <- imp0

# Generate a suite of diagnostic plots (returned as a list of ggplot objects)
plots <- rfgr_plot_suite(fit, se)

# Inspect available plots
names(plots)
```

---

shap_train_ranger — *Compute a SHAP matrix using a single ranger model*

Description

Trains a single probability random forest on the selected genes and computes per-sample SHAP values with fastshap. Rows = samples (colData rows), cols = genes.

Usage

```
shap_train_ranger(
  se,
  label_col = "state",
  genes,
  class_weights = NULL,
  num.trees = 500,
  seed = 1L,
  nsim = 64,
  pos_label = NULL
)
```

Arguments

`se`	SummarizedExperiment with assay "expr" (genes x samples).
`label_col`	Outcome column in colData(se) (factor).
`genes`	Character vector of gene IDs (must match rownames of assay(se,"expr")).
`class_weights`	Optional named numeric vector of class weights; if NULL, inverse-frequency weights are used.
`num.trees`	Number of trees (default 500).
`seed`	RNG seed.
`nsim`	fastshap Monte Carlo samples (default 64).
`pos_label`	Positive class label (defaults to level 2 of y).

Value

Numeric matrix of SHAP values (n_samples x length(genes)).

Examples

```
# For reproducibility, specify a fixed seed (e.g., set.seed(1)) before running this example.

# Toy feature matrix and binary outcome
X <- data.frame(
  x1 = stats::rnorm(20),
  x2 = stats::rnorm(20)
)
y <- factor(rep(c("A", "B"), each = 10))

# Inspect inputs
head(X)
```

---

sign_importance *Signed feature importance for RFGeneRank models*

Description

Add direction (+/-) to RF importance using group means ("mean"), external DE log2FC ("de"), or SHAP ("shap").

Usage

```
sign_importance(
  fit,
  X,
  y = NULL,
  method = c("mean", "de", "shap"),
  de_table = NULL,
  case_level = NULL,
  orientation = c("samples_by_genes", "genes_by_samples"),
  assay_name = NULL,
  shap_n = 50,
  seed = 1
)
```

Arguments

fit	Trained model object from rank_genes() or similar.
X	Expression (matrix/data.frame/SummarizedExperiment).
y	Factor labels (optional if retrievable from fit).
method	c("mean","de","shap"). Default "mean".

de_table	data.frame with columns gene, log2FC (for method="de").
case_level	Positive class label (default = last level of y).
orientation	"samples_by_genes" or "genes_by_samples".
assay_name	SE assay name/index.
shap_n	Integer; number of Monte Carlo samples for SHAP.
seed	RNG seed.

Value

data.frame with gene, importance, direction, signed_importance, mean_case, mean_ctrl, mean_diff, log2FC, shap_dir.

Examples

```
# Toy expression matrix: samples x genes
X <- matrix(
  rnorm(4 * 5),
  nrow = 4,
  dimnames = list(
    paste0("sample", 1:4),
    paste0("gene",   1:5)
  )
)

# Binary labels
y <- factor(c("Control", "Control", "Case", "Case"))

# Minimal "fit" object: a list with a numeric importance vector
fit <- list(
  importance = setNames(
    c(0.8, 0.6, 0.4, 0.2, 0.1),
    paste0("gene", 1:5)
  )
)

res <- sign_importance(
  fit = fit,
  X   = X,
  y   = y,
  method = "mean"
)

head(res)
# In practice, sign_importance() is called on a GeneRankFit object
# produced by the RFGeneRank workflow, for example:
#
#   fit <- gene_rank(se, genes = rownames(se), ...)
#   sig_imp <- sign_importance(fit, X = expr_matrix, y = outcome)
#   head(sig_imp)
```

top_genes — *Extract top predictive genes from a GeneRankFit*

Description

Returns a ranked list from the aggregated, fold-normalized importance stored in the fitted object. Optionally adds an ID mapping column (e.g., ENTREZID -> SYMBOL) using `id_map`.

Usage

```
top_genes(
  fit,
  n = 100,
  map = FALSE,
  OrgDb = org.Hs.eg.db::org.Hs.eg.db,
  from = "SYMBOL",
  to = "SYMBOL"
)
```

Arguments

`fit`	a `GeneRankFit` object (from `rank_genes()`).
`n`	integer; number of top genes to return (default 100).
`map`	logical; if TRUE, map `from` -> `to` and add a `mapped` column.
`OrgDb`	an `OrgDb` object for mapping (default `org.Hs.eg.db`).
`from`	source keytype used for the gene identifiers (e.g., "ENTREZID", "SYMBOL", "ENSEMBL").
`to`	destination keytype (e.g., "SYMBOL").

Value

A list with:

gene character vector of top gene IDs in `from` keytype

table data.frame with columns `gene`, `importance`, `SelectedInFolds`, and optional `mapped`

Examples

```
gene_scores <- data.frame(
  gene       = paste0("gene", 1:6),
  importance = c(5, 4, 3, 2, 1, 0)
)

fit <- methods::new("GeneRankFit", imp = gene_scores)

tg <- top_genes(fit, n = 3)
tg$gene
```

```
tg$table
# In practice, top_genes() is used on a GeneRankFit object.
# For example, after running a full RFGeneRank pipeline:
#
#   fit <- gene_rank(se, genes = rownames(se), ...)
#   head(top_genes(fit, n = 20))
#
# where 'fit' is a GeneRankFit containing gene importance scores.
```

---

validate_genes — *Validate a ranked gene set with alternate learners via k-fold CV*

Description

Validate a ranked gene set with alternate learners via k-fold CV

Usage

```
validate_genes(
  se,
  genes,
  methods = c("glmnet", "xgboost", "ranger"),
  k = 5,
  seed = 1L,
  model_params = list(),
  label_col = "state",
  positive = NULL,
  calibrate = c("platt", "isotonic", "none"),
  thr_metric = c("youden", "f1", "cost"),
  cost = c(fp = 1, fn = 1)
)
```

Arguments

se	A SummarizedExperiment whose assay is genes-by-samples.
genes	Character vector of gene IDs (must match `rownames(assay(se))`).
methods	Character vector; any of `c("ranger","glmnet","xgboost")`.
k	Integer number of folds (default 5).
seed	Integer RNG seed for reproducibility.
model_params	Named list of per-method parameter lists, e.g. `list( ranger = list(num.trees=1000, importance="none", nthread=1), glmnet = list(alpha=0.5, standardize="zscore", clip=8, eps_sd=1e-8, use_class_weights=TRUE, lambda="lambda.min"), xgboost = list(nrounds=400, eta=0.05, max_depth=4, nthread=1) )`.
label_col	Column name in `colData(se)` with the class labels. Must be a binary factor (exactly 2 levels).
positive	Optional; the positive class label. If `NULL`, uses `levels(y)[2]`.

calibrate	One of c("platt","isotonic","none"); applied per fold.
thr_metric	One of c("youden","f1","cost") for threshold selection.
cost	Named numeric vector c(fp=1, fn=1) if thr_metric == "cost".

Value

A list with $summary and one entry per method. Each entry contains: $oof (data.frame with p_raw, p_cal, p_use, y, fold), $calibrator_requested, $calibrator_used, $threshold, $conf_mat, and $metrics with both diagnostics (raw/cal) and final guardrailed metrics (auc_final, ece_final, brier_final).

Examples

```
# Toy expression matrix: 10 genes x 12 samples
expr <- matrix(
  stats::rnorm(10 * 12),
  nrow = 10,
  dimnames = list(
    paste0("gene", 1:10),
    paste0("sample", 1:12)
  )
)

# Binary labels as a factor (balanced)
label <- factor(rep(c("A", "B"), each = 6))

se <- SummarizedExperiment::SummarizedExperiment(
  assays  = list(expr = expr),
  colData = S4Vectors::DataFrame(label = label)
)

# Use the first 5 genes as a toy signature
genes <- rownames(expr)[1:5]

# Validate using ranger only (fast and robust for examples)
res <- validate_genes(
  se        = se,
  genes     = genes,
  methods   = "ranger",
  k         = 3,
  seed      = 1,
  label_col = "label"
)

# Inspect out-of-fold AUROC
res$summary$auc_final
```

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