

Package ‘panoramic’

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Title Meta-Analysis of Spatial Colocalization in Spatial Omics

Version 0.99.3

Description Provides a pipeline for quantifying and meta-analyzing spatial colocalization between cell types in spatial omics experiments. The package prepares SpatialExperiment inputs, computes Loh-bootstrap spatial summary functions (e.g. L- and K-functions) for cell-type pairs across samples, and performs random-effects meta-analysis to assess group-level differences in spatial colocalization.

URL <https://github.com/plevritis-lab/panoramic>

BugReports <https://github.com/plevritis-lab/panoramic/issues>

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.local_comp_score	<i>Internal: local composition enrichment score</i>
-------------------	---

Description

Internal: local composition enrichment score

Usage

```
.local_comp_score(frac, n_neighbors, overlap_area, global_density)
```

Value

Numeric vector of local enrichment scores (percentage-point difference between observed and expected local composition).

.lohboot_block_weighted

Internal: custom Loh bootstrap with overlap-weighted blocks

Description

Internal: custom Loh bootstrap with overlap-weighted blocks

Usage

```
.lohboot_block_weighted(  
  X,  
  fun = c("pcf", "Kest", "Lest", "pcfinhom", "Kinhom", "Linhom", "Kcross", "Lcross",  
    "Kdot", "Ldot", "Kcross.inhom", "Lcross.inhom"),  
  ...,  
  global = FALSE,  
  basicboot = FALSE,  
  Vcorrection = FALSE,  
  confidence = 0.95,  
  nx = 4,  
  ny = nx,  
  nsim = 200,  
  type = 7  
)
```

Arguments

X	A marked ppp object.
fun	Character/function passed to spatstat local summary mapping.
...	Additional arguments forwarded to the selected local function.
global	Logical; if TRUE, compute global envelopes.
basicboot	Logical; if TRUE, use basic bootstrap intervals.
Vcorrection	Logical; apply variance correction for K-type functions.
confidence	Numeric confidence level in (0.5, 1).
nx, ny	Integer numbers of blocks in x/y for block bootstrap.
nsim	Integer bootstrap replicates.
type	Quantile type.

Value

A data.frame with columns including r, theoretical curve, estimate, and lower/upper interval bounds.

.lohboot_local_comp *Internal: Loh-style bootstrap for local composition enrichment*

Description

Internal: Loh-style bootstrap for local composition enrichment

Usage

```
.lohboot_local_comp(
  X,
  from,
  to,
  radii_um,
  nsim = 200,
  confidence = 0.95,
  type = 7,
  boot = c("approx", "block"),
  nx = 4,
  ny = nx,
  local_cache = NULL
)
```

Arguments

<code>X</code>	A marked ppp object.
<code>from, to</code>	Character marks defining anchor and target cell types.
<code>radii_um</code>	Numeric radii at which enrichment is evaluated.
<code>nsim</code>	Integer bootstrap replicates.
<code>confidence</code>	Numeric confidence level.
<code>type</code>	Quantile type for bootstrap intervals.
<code>boot</code>	One of "approx" or "block".
<code>nx, ny</code>	Integer block counts (used only for <code>boot = "block"</code>).
<code>local_cache</code>	Optional cache from <code>.precompute_local_comp_cache()</code> .

Value

A data.frame compatible with `.summarize_lohboot()`.

.lohboot_quiet *Internal: quiet Loh bootstrap wrapper*

Description

Run `spatstat.explore::lohboot()` while suppressing console output, returning the bootstrap object invisibly for further summarization.

Usage

```
.lohboot_quiet(  
  X,  
  fun,  
  ...,  
  verbose = FALSE,  
  boot = c("approx", "block"),  
  tile_size = NULL,  
  nx = NULL,  
  ny = NULL  
)
```

Arguments

...	Arguments passed to <code>spatstat.explore::lohboot()</code> .
boot	Character. Bootstrap mode: "approx" (no tiling) or "block" (tiled Loh bootstrap with overlap-weighted blocks).
tile_size	Optional numeric scalar giving tile size in the same units as spatial coordinates. Used only when <code>boot = "block"</code> ; translated into <code>nx</code> and <code>ny</code> for <code>lohboot()</code> based on the sample's window bounding box. Cannot be used with <code>nx/ny</code> .
nx, ny	Optional integers giving the number of tiles in x/y directions for <code>lohboot()</code> when <code>boot = "block"</code> . Ignored for <code>boot = "approx"</code> .

Value

A Loh bootstrap object as returned by `spatstat.explore::lohboot()` or a compatible `data.frame` for `boot = "block"`.

.one_pair_one_sample *Internal: compute spatial stats for one pair in one sample*

Description

Compute a spatial summary curve and bootstrap variance for a single cell-type pair within a single prepared sample, evaluated on a common radius grid.

Usage

```
.one_pair_one_sample(
  meta,
  ct1,
  ct2,
  stat = "local_comp_enrichment",
  nsim = 100,
  correction = "translate",
  radii_um,
  verbose = FALSE,
  boot = c("approx", "block"),
  tile_size = NULL,
  nx = NULL,
  ny = NULL,
  local_comp_cache = NULL
)
```

Arguments

<code>meta</code>	The <code>metadata\$panoramic</code> list for one sample, containing at least a <code>spatstat</code> ppp object and a <code>marks_tab</code> table.
<code>ct1, ct2</code>	Character. Cell-type labels.
<code>stat</code>	Character. Summary statistic. Default is <code>"local_comp_enrichment"</code> . Other options are <code>"Lcross"</code> , <code>"Kcross"</code> , <code>"Lest"</code> , and <code>"Kest"</code> .
<code>nsim</code>	Integer. Number of Loh bootstrap simulations.
<code>correction</code>	Character. Edge correction passed to <code>spatstat</code> .
<code>radii_um</code>	Numeric vector of radii (microns) on which to summarize.
<code>boot</code>	Character. Bootstrap mode: <code>"approx"</code> (no tiling) or <code>"block"</code> (tiled Loh bootstrap).
<code>tile_size</code>	Optional numeric scalar giving tile size in the same units as spatial coordinates. Used only when <code>boot = "block"</code> .
<code>nx, ny</code>	Optional integers giving the number of tiles in x/y directions when <code>boot = "block"</code> .
<code>local_comp_cache</code>	Optional cache object from <code>.precompute_local_comp_cache()</code> to avoid repeated neighbor searches when <code>stat = "local_comp_enrichment"</code> .

Value

A data.frame with columns `radius_um`, `yi`, and `vi`, filled with NA if insufficient cells of either type are present.

`.panoramic_add_coloc_direction`

Internal: add directional colocalization labels

Description

Internal: add directional colocalization labels

Usage

```
.panoramic_add_coloc_direction(df)
```

.panoramic_attach_sample_metadata

Internal: attach sample-level metadata to PANORAMIC colData

Description

Internal: attach sample-level metadata to PANORAMIC colData

Usage

```
.panoramic_attach_sample_metadata(se_stats, spe_list, fields)
```

Arguments

<code>se_stats</code>	SummarizedExperiment from <code>panoramic_spatialstats()</code> .
<code>spe_list</code>	Named list of SpatialExperiment objects used to produce <code>se_stats</code> .
<code>fields</code>	Character vector of colData fields to attach.

Value

`se_stats` with additional columns in `colData(se_stats)`.

.panoramic_extract_meta_table

Internal: extract feature-level meta-analysis table from rowData

Description

Internal: extract feature-level meta-analysis table from rowData

Usage

```
.panoramic_extract_meta_table(  
  se,  
  feature_cols = c("ct1", "ct2", "radius_um", "stat"),  
  drop_na = FALSE  
)
```

```
.panoramic_extract_spatialstats_table
```

Internal: flatten spatialstats assays to a long table

Description

Internal: flatten spatialstats assays to a long table

Usage

```
.panoramic_extract_spatialstats_table(se, drop_na = FALSE)
```

```
.panoramic_one_value_per_sample
```

Internal: extract one metadata value per sample from a SpatialExperiment list

Description

Internal: extract one metadata value per sample from a SpatialExperiment list

Usage

```
.panoramic_one_value_per_sample(spe_list, field)
```

Arguments

spe_list	Named list of SpatialExperiment objects.
field	Character scalar naming a colData column in each sample.

Value

Character vector aligned to names(spe_list), one value per sample.

```
.panoramic_pairs
```

Internal: generate cell-type pairs

Description

Construct the set of cell-type pairs to analyze, optionally including self-pairs and filtering to cell types present in at least a given fraction of samples.

Usage

```
.panoramic_pairs(prepare_list, include_self = TRUE, min_presence = 0)
```

Arguments

- prep_list List of prepared SpatialExperiment objects, each with metadata(spe)\$panoramic\$ppp containing a marked spatstat point pattern.
- include_self Logical. If TRUE, include (ct, ct) self-pairs. If FALSE, only cross-type pairs are returned.
- min_presence Numeric in [0, 1]. Minimum fraction of samples in which a cell type must be observed (at least one cell) to be included. 0 keeps all observed types, 0.5 requires observed presence in at least half of samples.

Value

A data.frame with columns ct1 and ct2.

.precompute_local_comp_cache

Internal: precompute local composition enrichment cache

Description

Build per-radius local composition enrichment matrices for a point pattern. For each point and radius, store local neighbor fractions/counts and the overlap area between the radius-disc and tissue window so enrichment can be computed as an edge-corrected proportion difference.

Usage

.precompute_local_comp_cache(X, radii_um)

Arguments

- X A marked ppp object.
- radii_um Numeric radii at which to precompute local composition.

Value

A list containing precomputed local composition matrices and indexing structures used by local composition bootstrap routines.

.reorder_ccw

Internal: reorder hull vertices counterclockwise Orders a set of 2D coordinates counterclockwise around their centroid. Mainly used for convex spatial window construction to ensure correct polygon orientation for spatstat owin objects.

Description

Internal: reorder hull vertices counterclockwise Orders a set of 2D coordinates counterclockwise around their centroid. Mainly used for convex spatial window construction to ensure correct polygon orientation for spatstat owin objects.

Usage

```
.reorder_ccw(coords)
```

Arguments

coords Numeric matrix of coordinates (columns: x, y).

Value

Reordered numeric matrix of coordinates

.safe_approx *Internal: safe interpolation on a common radius grid*

Description

Interpolate values y at target x_{out} using `stats::aprox()`, handling missing/non-finite values and low sample sizes.

Usage

```
.safe_approx(x, y, xout)
```

Arguments

x Numeric vector of original inputs x .
 y Numeric vector of original y -values.
 x_{out} Numeric vector of target x -values.

Value

Numeric vector of interpolated values, length `length(xout)`.

.spatstat_local_function_info
Internal: local function info (spatstat helper)

Description

Internal: local function info (spatstat helper)

Usage

```
.spatstat_local_function_info(key)
```

Arguments

key Character scalar naming a supported spatstat summary function.

Value

A named list describing the global/local function mapping and options for the requested key, or NULL if unsupported.

<code>.summarize_lohboot</code>	<i>Internal: summarize Loh bootstrap to (r, yi, vi)</i>
---------------------------------	---

Description

Convert a spatstat Loh bootstrap object to aligned vectors of radii, centered estimates, and variance. Variance is taken directly if present, reconstructed from confidence intervals if needed, or computed from simulation replicates as a fallback.

Usage

```
.summarize_lohboot(loh_obj, center_L = TRUE, conf = 0.95)
```

Arguments

<code>loh_obj</code>	Loh bootstrap object returned by spatstat's L/K-summary functions with <code>global=TRUE</code> .
<code>center_L</code>	Logical. If TRUE, center the estimate by the theoretical curve (e.g. $L(r)-r$) when available.
<code>conf</code>	Numeric confidence level used when reconstructing variance from confidence interval half-width.

Value

A data.frame with numeric columns `r`, `yi`, and `vi`, or NULL if the object cannot be parsed.

<code>create_spatial_network</code>	<i>Construct spatial colocalization network from PANORAMIC results</i>
-------------------------------------	--

Description

Build a cell-type network where edges represent differential spatial colocalization between cell-type pairs, based on the output of `panoramic_meta_mv(...)` (or a compatible function). Edges are filtered by FDR and optional `z_diff` sign, and weighted by $|z_diff|$.

Usage

```
create_spatial_network(
  se_diff,
  fdr_threshold = 0.05,
  leiden_resolution = 1,
  z_sign = c("both", "positive", "negative"),
  include_nonsig = FALSE,
  nonsig_max_fdr = 1,
  directed = FALSE,
  sig_operator = c("lt", "gt")
)
```

Arguments

<code>se_diff</code>	A SummarizedExperiment returned by <code>panoramic_meta_mv(...)</code> , where <code>rowData(se_diff)</code> contains at least <code>ct1</code> , <code>ct2</code> , <code>z_diff</code> , <code>p_diff</code> , and <code>fdr_diff</code> .
<code>fdr_threshold</code>	Numeric scalar. FDR threshold used to define significance for <code>edge_class</code> and, when <code>include_nonsig = FALSE</code> , to filter edges (default 0.05).
<code>leiden_resolution</code>	Numeric. Clustering resolution for the Leiden algorithm.
<code>z_sign</code>	Character sign filter for <code>z_diff</code> , one of "both" (default), "positive", or "negative". This enables group-specific networks by retaining only positive or only negative differential effects.
<code>include_nonsig</code>	Logical. If TRUE, include non-significant edges (up to <code>nonsig_max_fdr</code>) and mark them as dotted in plotting. If FALSE (default), keep only <code>fdr_diff < fdr_threshold</code> .
<code>nonsig_max_fdr</code>	Numeric upper bound for retained edges when <code>include_nonsig = TRUE</code> (default 1.0).
<code>directed</code>	Logical. If TRUE, construct a directed network (and directed centrality metrics). If FALSE, construct an undirected network.
<code>sig_operator</code>	One of "lt" (default) or "gt" controlling significance threshold direction for <code>fdr_diff</code> when <code>include_nonsig = FALSE</code> . "lt" uses standard <code>fdr_diff < fdr_threshold</code> ; "gt" inverts the threshold (diagnostic use only).

Value

A list with components:

- `graph`: an igraph object (directed or undirected) with edge attributes `weight`, `fdr`, `pval`, `edge_sig`, `edge_class` and vertex attributes `cluster`, `cluster_id`, `degree`, `betweenness`, `strength`.
- `clusters`: the community structure object from `igraph::cluster_leiden()`.
- `n_clusters`: number of detected clusters.
- `modularity`: modularity score of the clustering.
- `z_sign`: the applied sign filter.
- `fdr_threshold`: the applied significance threshold.
- `include_nonsig`: whether non-significant edges were included.
- `nonsig_max_fdr`: maximum retained FDR when non-significant edges are included.

Examples

```
se_diff <- SummarizedExperiment::SummarizedExperiment(
  assays = list(dummy = matrix(0, nrow = 3, ncol = 1)),
  rowData = S4Vectors::DataFrame(
    ct1 = c("A", "A", "B"),
    ct2 = c("B", "C", "C"),
    z_diff = c(2.0, -1.5, 1.2),
    p_diff = c(0.01, 0.03, 0.20),
    fdr_diff = c(0.02, 0.05, 0.30)
  )
)
```

```

net <- create_spatial_network(
  se_diff,
  fdr_threshold = 0.2,
  z_sign = "both",
  include_nonsig = TRUE
)

net$graph

```

null_coalesce	<i>Pipe-compatible null operator</i>
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Description

Returns b if a is NULL, otherwise a.

Usage

```
a %||% b
```

Arguments

a b Objects to test; if a is NULL b is returned.

Value

The non-NULL object.

panoramic	<i>Run PANORAMIC End-To-End</i>
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Description

panoramic_analyze() runs preparation, spatial statistics, and multilevel pooling in one call. panoramic() is a convenience alias with identical arguments and return structure.

Usage

```

panoramic(
  spe_list,
  design,
  cell_type = "cell_type",
  pairs = "auto",
  radii_um,
  stat = "local_comp_enrichment",
  nsim = 100,
  correction = NULL,
  min_cells = 5L,
  concavity = 50,
  window = c("concave", "convex", "rect"),

```

```

group_col = "group",
group_tau2 = c("none", "separate"),
patient_col = NULL,
sample_col = NULL,
tau_structure = c("patient", "patient_sample"),
method_mv = "REML",
vi_floor = "group_median",
seed = 123,
boot = c("approx", "block"),
tile_size = NULL,
nx = NULL,
ny = NULL,
BPPARAM = BiocParallel::SerialParam(),
verbose = FALSE
)

```

Arguments

spe_list	Named list of SpatialExperiment objects (one per sample).
design	data.frame with at least columns sample and group.
cell_type	Character colData column containing cell-type labels.
pairs	Either "auto" or a data.frame with columns ct1, ct2.
radii_um	Numeric vector of radii (microns).
stat	Spatial statistic passed to panoramic_spatialstats().
nsim	Integer bootstrap replicates per sample/pair.
correction	Optional edge-correction method for spatstat-based statistics. Ignored when stat = "local_comp_enrichment".
min_cells	Minimum cells per type per sample during preparation.
concavity	Concavity for concave-hull sample windows (larger values approach convex hulls).
window	One of "concave", "convex", or "rect".
group_col	Group column in colData used for multilevel pooling and contrasts.
group_tau2	If "separate", fit additional per-group multilevel models to report group-specific heterogeneity components.
patient_col	Optional patient-id column for multilevel pooling. If NULL, PANORAMIC uses "patient" from design when available, otherwise falls back to sample_col.
sample_col	Optional sample-id column used in panoramic_meta_mv(). If NULL, PANORAMIC uses "sample" (aligned to design\$sample).
tau_structure	Random-effects structure in panoramic_meta_mv(): "patient" or "patient_sample".
method_mv	Estimator passed to metafor::rma.mv() (for example "REML").
vi_floor	Variance-flooring mode passed to panoramic_meta_mv(). Default is "group_median" ("median", "group_median", or "none").
seed	Optional random seed for reproducibility.
boot	Bootstrap mode in panoramic_spatialstats(): "approx" or "block".
tile_size	Optional tile size for block bootstrap (same units as coordinates).
nx, ny	Optional tile counts for block bootstrap (used when boot = "block").
BPPARAM	BiocParallel backend.
verbose	Logical verbosity passed to bootstrap routines.

Details

panoramic() delegates directly to panoramic_analyze().

Value

A list with:

- prep: output of panoramic_prepare().
- stats: output of panoramic_spatialstats().
- pooled: output of panoramic_meta_mv().
- tables: pre-flattened data.frames (spatialstats/meta/contrast).

Examples

```
toy <- panoramic_simulate_dataset(seed = 1)
out <- panoramic(
  spe_list = toy$spe_list,
  design = toy$design,
  cell_type = "cell_type",
  radii_um = c(10, 20),
  nsim = 5,
  min_cells = 2,
  window = "rect",
  BPPARAM = BiocParallel::SerialParam()
)
names(out)
```

panoramic_analyze

Run PANORAMIC end-to-end, including pooling/meta-analysis

Description

panoramic_analyze() provides a streamlined API for the most common workflow: prepare data, compute spatial statistics, and run pooling/meta-analysis in one call.

Usage

```
panoramic_analyze(
  spe_list,
  design,
  cell_type = "cell_type",
  pairs = "auto",
  radii_um,
  stat = "local_comp_enrichment",
  nsim = 100,
  correction = NULL,
  min_cells = 5L,
  concavity = 50,
  window = c("concave", "convex", "rect"),
  group_col = "group",
  group_tau2 = c("none", "separate"),
```

```

patient_col = NULL,
sample_col = NULL,
tau_structure = c("patient", "patient_sample"),
method_mv = "REML",
vi_floor = "group_median",
seed = 123,
boot = c("approx", "block"),
tile_size = NULL,
nx = NULL,
ny = NULL,
BPPARAM = BiocParallel::SerialParam(),
verbose = FALSE
)

```

Arguments

spe_list	Named list of SpatialExperiment objects (one per sample).
design	data.frame with at least columns sample and group.
cell_type	Character; colData column containing cell-type labels.
pairs	Either "auto" or a data.frame with columns ct1, ct2.
radii_um	Numeric vector of radii in microns.
stat	Character spatial statistic passed to panoramic_spatialstats().
nsim	Integer bootstrap replicates.
correction	Optional edge-correction method for spatstat-based statistics. Ignored when stat = "local_comp_enrichment".
min_cells	Minimum cells per type per sample.
concavity	Concavity for concave hull windows.
window	One of "concave", "convex", or "rect".
group_col	Character group column for meta-analysis (defaults to "group").
group_tau2	Controls whether PANORAMIC additionally computes group-specific heterogeneity (tau2) by fitting per-group multilevel models. Use "none" for faster fitting or "separate" for more detailed heterogeneity summaries.
patient_col	Optional patient-id column for multilevel pooling. If NULL, PANORAMIC uses "patient" from design when available, otherwise falls back to sample_col.
sample_col	Optional sample-id column used in panoramic_meta_mv(). If NULL, PANORAMIC uses "sample" (aligned to design\$sample).
tau_structure	Random-effects structure passed to panoramic_meta_mv().
method_mv	Method passed to metafor::rma.mv() in panoramic_meta_mv().
vi_floor	Variance-flooring mode in panoramic_meta_mv(). Default is "group_median". Use "median" to replace non-positive vi with per-feature median positive vi, or "none" to disable flooring.
seed	Optional random seed.
boot	Bootstrap mode "approx" or "block".
tile_size	Optional tile size for block bootstrap.
nx, ny	Optional tile counts for block bootstrap.
BPPARAM	BiocParallel backend.
verbose	Logical verbosity passed to panoramic_spatialstats().

Value

A list with:

- prep: output of panoramic_prepare()
- stats: output of panoramic_spatialstats()
- pooled: output of panoramic_meta_mv()
- tables: pre-flattened data.frames for convenient result extraction

Examples

```
toy <- panoramic_simulate_dataset(seed = 1)
out <- panoramic_analyze(
  spe_list = toy$spe_list,
  design = toy$design,
  cell_type = "cell_type",
  radii_um = c(10, 20),
  stat = "local_comp_enrichment",
  nsim = 5,
  min_cells = 2,
  window = "rect",
  group_col = "group",
  BPPARAM = BiocParallel::SerialParam()
)
names(out)
```

panoramic_extract_contrast

Extract PANORAMIC Contrast, Meta, or Spatialstats Tables

Description

Convenience helper for flattening PANORAMIC outputs into analysis-ready tables.

Usage

```
panoramic_extract_contrast(
  se,
  feature_cols = c("ct1", "ct2", "radius_um"),
  what = c("contrast", "meta", "spatialstats"),
  drop_na = FALSE
)
```

Arguments

se	A SummarizedExperiment from PANORAMIC workflow steps.
feature_cols	Feature columns to include when available (for example ct1, ct2, radius_um).
what	Which table to extract: "contrast", "meta", or "spatialstats".
drop_na	If TRUE, drop rows with missing extracted statistics.

Value

A data.frame. For what = "contrast", the table includes beta_diff, se_diff, z_diff, p_diff, and fdr_diff, plus available feature columns.

Examples

```
se <- SummarizedExperiment::SummarizedExperiment(
  assays = list(dummy = matrix(0, nrow = 1, ncol = 1)),
  rowData = S4Vectors::DataFrame(
    ct1 = "A",
    ct2 = "B",
    radius_um = 10,
    beta_diff = 0.25,
    se_diff = 0.10,
    z_diff = 2.5,
    p_diff = 0.012,
    fdr_diff = 0.02
  )
)

panoramic_extract_contrast(se)
```

panoramic_meta_mv

Multilevel Random-Effects Meta-Analysis of PANORAMIC Features

Description

Feature-wise multilevel random-effects pooling for PANORAMIC spatial statistics using `metafor::rma.mv()`, accounting for clustering of samples within patients.

Usage

```
panoramic_meta_mv(
  se,
  patient_col,
  group_col = NULL,
  sample_col = "sample",
  tau_structure = c("patient", "patient_sample"),
  method = "REML",
  group_tau2 = c("none", "separate"),
  warn_sigma2 = TRUE,
  vi_floor = NULL,
  sigma2_tol = 1e-06,
  sigma2_rel = 1e-04,
  control = NULL,
  sparse = FALSE,
  BPPARAM = BiocParallel::SerialParam()
)
```

Arguments

se	A SummarizedExperiment with assays yi and vi.
patient_col	Column in colData(se) identifying patients.
group_col	Optional grouping column. When provided, pooled means are estimated with $\text{mods} = \sim 0 + \text{group}$. For two groups, contrast is $\text{beta_diff} = \text{group2} - \text{group1}$; group order is factor levels (if factor) or lexicographic order of labels.
sample_col	Optional sample-id column; if NULL, colnames(se) are used.
tau_structure	Random-effects structure: "patient" or "patient_sample".
method	Estimator passed to metafor::rma.mv() (for example "REML").
group_tau2	If "separate", additionally fit per-group multilevel models to estimate group-specific heterogeneity components.
warn_sigma2	If TRUE, warn when many features have near-zero variance components.
vi_floor	Optional handling for non-positive vi: "median", "group_median", or "none".
sigma2_tol	Absolute tolerance for near-zero sigma2 diagnostics.
sigma2_rel	Relative tolerance (fraction of median vi) for near-zero sigma2 diagnostics.
control	Optional named optimizer control list passed to metafor::rma.mv().
sparse	Logical forwarded to metafor::rma.mv(sparse = ...).
BPPARAM	BiocParallel backend used across features.

Value

The input SummarizedExperiment with meta-analysis columns appended to rowData(se). For grouped analyses, columns are group-prefixed (*_mu_hat, *_se_mu, *_p_mu, *_k). For exactly two groups, contrast columns beta_diff, se_diff, z_diff, p_diff, fdr_diff are added. Metadata are stored in metadata(se)\$panoramic\$meta_mv.

Examples

```

yi <- matrix(c(0.20, 0.15, 0.10, 0.05), nrow = 1)
vi <- matrix(c(0.04, 0.05, 0.06, 0.05), nrow = 1)
colnames(yi) <- colnames(vi) <- paste0("s", seq_len(4L))

se <- SummarizedExperiment::SummarizedExperiment(
  assays = list(yi = yi, vi = vi),
  rowData = S4Vectors::DataFrame(ct1 = "A", ct2 = "B", radius_um = 10),
  colData = S4Vectors::DataFrame(
    sample = paste0("s", seq_len(4L)),
    patient = paste0("p", seq_len(4L)),
    group = c("control", "control", "case", "case")
  )
)

se_mv <- panoramic_meta_mv(
  se = se,
  patient_col = "patient",
  group_col = "group",
  sample_col = "sample",
  BPPARAM = BiocParallel::SerialParam()
)

SummarizedExperiment::rowData(se_mv)$beta_diff

```

panoramic_prepare *Prepare PANORAMIC inputs from a list of SpatialExperiment objects*

Description

Creates SpatialExperiment objects ready for PANORAMIC spatial analyses. Cell type labels are harmonized, rare cell types (fewer than min_cells) are dropped per sample, and a spatial window is computed. Cached spatstat objects are stored within each SpatialExperiment's metadata.

Usage

```
panoramic_prepare(
  spe_list,
  design,
  cell_type = "cell_type",
  min_cells = 5,
  concavity = 50,
  window = c("concave", "convex", "rect"),
  BPPARAM = BiocParallel::SerialParam()
)
```

Arguments

spe_list	Named or unnamed list of SpatialExperiment (one per sample)
design	data.frame with at least columns sample, group to map samples for meta-analysis. If only one group is used, give all the same group label.
cell_type	Character; name of SpatialExperiment colData column holding cell type labels
min_cells	Integer. Cell types with fewer than this count (per sample) are dropped.
concavity	Numeric passed to concaveman::concaveman(). Controls level of hull detail. 1 is highly detailed, Inf is a convex hull.
window	one of "concave", "convex", "rect". Typically use concave.
BPPARAM	BiocParallel param for optional parallel processing.

Details

This step computes per-sample spatial windows to exclude background, filters rare cell types separately per sample, builds consistent cell-type factor levels, and caches spatstat objects and type tables for PANORAMIC's spatial statistics.

Value

List of SpatialExperiment objects with metadata slot panoramic containing ppp, cell-type table, spatial window, group/sample info.

Examples

```

spe_list <- list(
  sample1 = panoramic_simulate_spe(
    n_cells = 60,
    sample_id = "sample1",
    scenario = "random",
    seed = 1
  )
)

# Design with a single group -----
design <- data.frame(
  sample = "sample1",
  group = "group1",
  stringsAsFactors = FALSE
)

# Run panoramic_prepare -----
prepped <- panoramic_prepare(
  spe_list,
  design = design,
  cell_type = "cell_type",
  min_cells = 3,
  concavity = 50,
  window = "concave",
  BPPARAM = BiocParallel::SerialParam()
)

# Inspect cached spatstat objects in metadata
names(S4Vectors::metadata(prepped[[1]])$panoramic)

```

panoramic_simulate_dataset

Simulate a two-group PANORAMIC example dataset

Description

Create a list of SpatialExperiment objects and matching design table for differential colocalization tutorials.

Usage

```

panoramic_simulate_dataset(
  n_group1 = 3L,
  n_group2 = 3L,
  n_cells_group1 = 200L,
  n_cells_group2 = 350L,
  group_labels = c("group1", "group2"),
  scenario_group1 = "random",
  scenario_group2 = "colocalized",
  seed = NULL
)

```

Arguments

n_group1	Integer number of samples in group 1.
n_group2	Integer number of samples in group 2.
n_cells_group1	Integer number of cells per group-1 sample.
n_cells_group2	Integer number of cells per group-2 sample.
group_labels	Character length-2 vector of group names.
scenario_group1	Scenario passed to panoramic_simulate_spe() for group 1.
scenario_group2	Scenario passed to panoramic_simulate_spe() for group 2.
seed	Optional integer seed for reproducibility.

Value

A list with entries spe_list and design.

Examples

```
toy <- panoramic_simulate_dataset(seed = 1)
names(toy)
head(toy$design)
```

panoramic_simulate_spe

Simulate one SpatialExperiment object for PANORAMIC examples

Description

Create a toy SpatialExperiment with simple spatial patterns that can be used in package examples, vignettes, and tests.

Usage

```
panoramic_simulate_spe(
  n_cells = 200L,
  sample_id = "sample_1",
  cell_types = c("A", "B", "C"),
  scenario = c("random", "colocalized"),
  bounds = c(0, 100),
  center = c(50, 50),
  cluster_sd = 18,
  n_genes = 10L,
  seed = NULL
)
```

Arguments

n_cells	Integer number of cells to simulate.
sample_id	Character sample identifier stored in colData.
cell_types	Character vector of cell-type labels.
scenario	Character string, either "random" or "colocalized". In "colocalized", the first two cell types are enriched near the center.
bounds	Numeric length-2 vector giving minimum and maximum coordinate.
center	Numeric length-2 vector giving center for colocalized pattern.
cluster_sd	Numeric standard deviation for central clustering.
n_genes	Integer number of toy genes in the counts matrix.
seed	Optional integer for reproducibility.

Value

A SpatialExperiment object with simulated coordinates and cell types.

Examples

```
spe <- panoramic_simulate_spe(
  n_cells = 120,
  sample_id = "sample_1",
  scenario = "colocalized",
  seed = 1
)
spe
```

panoramic_spatialstats

Compute Pairwise Spatial Statistics for PANORAMIC

Description

Compute pairwise spatial summary curves and bootstrap variances across samples for all requested cell-type pairs and radii.

Usage

```
panoramic_spatialstats(
  prep,
  pairs = "auto",
  radii_um,
  stat = "local_comp_enrichment",
  nsim = 100,
  correction = "translate",
  seed = 123,
  boot = c("approx", "block"),
  tile_size = NULL,
  nx = NULL,
```

```

ny = NULL,
BPPARAM = BiocParallel::SerialParam(),
verbose = FALSE
)

```

Arguments

prep	List of prepared SpatialExperiment objects from panoramic_prepare().
pairs	Either "auto" or a data.frame with columns ct1, ct2.
radii_um	Numeric vector of radii (microns).
stat	Summary statistic. Default is "local_comp_enrichment". Other supported values are "Lcross", "Kcross", "Lest", and "Kest".
nsim	Integer number of Loh bootstrap replicates per sample/pair.
correction	Edge correction method passed to spatstat summaries.
seed	Optional seed for reproducible bootstrap sampling.
boot	Bootstrap mode: "approx" or "block".
tile_size	Optional tile size for block bootstrap in coordinate units.
nx, ny	Optional tile counts for block bootstrap when boot = "block".
BPPARAM	BiocParallel backend used across samples.
verbose	If TRUE, show bootstrap console output.

Details

For L-function statistics, PANORAMIC computes variances via the delta method from corresponding K-function bootstrap estimates and centers by r .

For `stat = "local_comp_enrichment"`, PANORAMIC reports edge-corrected observed-minus-expected local target composition (percentage points) and uses Loh bootstrap for uncertainty.

Value

A SummarizedExperiment with assays:

- y_i : centered estimates per (ct1, ct2, radius_um) feature and sample.
- v_i : variance estimates aligned to y_i .

rowData contains ct1, ct2, radius_um, stat; colData contains sample and group.

Examples

```

toy <- panoramic_simulate_dataset(seed = 1)
prep <- panoramic_prepare(
  spe_list = toy$spe_list,
  design = toy$design,
  cell_type = "cell_type",
  min_cells = 2,
  window = "rect",
  BPPARAM = BiocParallel::SerialParam()
)
se_stats <- panoramic_spatialstats(
  prep = prep,
  radii_um = c(10, 20),

```

```

    nsim = 5,
    correction = "translate",
    seed = 1,
    BPPARAM = BiocParallel::SerialParam()
  )
  se_stats

```

plot_forest

Forest Plot for PANORAMIC Spatial Colocalization

Description

Draw individual-sample estimates and pooled group estimates for one cell-type pair at one radius.

Usage

```

plot_forest(
  se_meta,
  ct1,
  ct2,
  radius_um = NULL,
  group_col = "group",
  group_colors = NULL,
  text_size = 2,
  header_text_size = 2,
  title_text_size = 8,
  base_size = 5,
  show_est_se = TRUE,
  show_ci = TRUE
)

```

Arguments

se_meta	SummarizedExperiment from panoramic_meta_mv() containing yi/vi assays and pooled columns in rowData.
ct1, ct2	Cell-type labels selecting one feature.
radius_um	Radius (microns). If NULL, the first available radius for the pair is used.
group_col	Group column in colData(se_meta).
group_colors	Optional named color vector for groups.
text_size	Text size for row annotations.
header_text_size	Text size for table-like column headers.
title_text_size	Title text size.
base_size	Base size passed to theme_classic().
show_est_se	Show the Est (SE) text column.
show_ci	Show the 95% CI text column.

Details

This helper currently supports exactly two groups in group_col.

Value

A ggplot forest-plot object.

Examples

```
yi <- matrix(c(0.12, 0.18, 0.35, 0.30), nrow = 1)
vi <- matrix(c(0.03, 0.04, 0.05, 0.05), nrow = 1)
colnames(yi) <- colnames(vi) <- paste0("s", seq_len(4L))

se_meta <- SummarizedExperiment::SummarizedExperiment(
  assays = list(yi = yi, vi = vi),
  rowData = S4Vectors::DataFrame(
    ct1 = "A",
    ct2 = "B",
    radius_um = 10,
    control_mu_hat = 0.15,
    control_se_mu = 0.10,
    case_mu_hat = 0.32,
    case_se_mu = 0.11
  ),
  colData = S4Vectors::DataFrame(
    group = c("control", "control", "case", "case")
  )
)

p <- plot_forest(
  se_meta,
  ct1 = "A",
  ct2 = "B",
  radius_um = 10,
  group_col = "group"
)

p
```

plot_representative_samples

Plot Representative Samples for Significant Differential Hits

Description

Select representative samples per group for significant differential colocalization features, then build side-by-side spatial panels highlighting source and target cell types.

Usage

```
plot_representative_samples(
  se_stats,
  se_meta,
```

```

    spe_list,
    top_hits = NULL,
    sig_col = c("fdr_diff", "p_diff"),
    alpha = 0.05,
    top_n = 10L,
    group_col = "group",
    cell_type_col = "cell_type",
    sample_col = "sample",
    out_prefix = NULL
  )

```

Arguments

<code>se_stats</code>	A SummarizedExperiment from <code>panoramic_spatialstats()</code> containing sample-level <code>yi</code> .
<code>se_meta</code>	A SummarizedExperiment from <code>panoramic_meta_mv()</code> containing contrast columns.
<code>spe_list</code>	Named list of <code>SpatialExperiment</code> objects.
<code>top_hits</code>	Optional data.frame of selected features. If <code>NULL</code> , features are selected from <code>se_meta</code> using <code>sig_col</code> , <code>alpha</code> , and <code>top_n</code> .
<code>sig_col</code>	One of <code>"fdr_diff"</code> or <code>"p_diff"</code> used when selecting <code>top_hits = NULL</code> .
<code>alpha</code>	Numeric threshold for feature selection when <code>top_hits = NULL</code> .
<code>top_n</code>	Integer number of selected hits when <code>top_hits = NULL</code> .
<code>group_col</code>	Character group column in <code>colData(se_stats)</code> .
<code>cell_type_col</code>	Character cell-type column in <code>colData(spe)</code> .
<code>sample_col</code>	Character sample-id column in <code>colData(se_stats)</code> .
<code>out_prefix</code>	Optional output prefix. If provided, each panel is saved as PNG/PDF and the returned index includes file paths.

Details

This helper currently supports exactly two groups in `group_col`.

Value

A list with plots (named list of `ggplot` objects) and index (data.frame summarizing selected hits and samples).

Examples

```

sample_ids <- paste0("sample_", seq_len(4L))
spe_list <- stats::setNames(
  lapply(sample_ids, function(sid) {
    panoramic_simulate_spe(
      n_cells = 40,
      sample_id = sid,
      cell_types = c("A", "B"),
      scenario = "random",
      seed = 1
    )
  })
, sample_ids

```

```

)

yi <- matrix(c(0.10, 0.15, 0.25, 0.30), nrow = 1)
vi <- matrix(rep(0.05, 4), nrow = 1)
colnames(yi) <- colnames(vi) <- sample_ids
se_stats <- SummarizedExperiment::SummarizedExperiment(
  assays = list(yi = yi, vi = vi),
  rowData = S4Vectors::DataFrame(ct1 = "A", ct2 = "B", radius_um = 10),
  colData = S4Vectors::DataFrame(
    sample = sample_ids,
    group = c("control", "control", "case", "case")
  )
)

se_meta <- SummarizedExperiment::SummarizedExperiment(
  assays = list(dummy = matrix(0, nrow = 1, ncol = 1)),
  rowData = S4Vectors::DataFrame(
    ct1 = "A",
    ct2 = "B",
    radius_um = 10,
    beta_diff = 0.25,
    se_diff = 0.10,
    z_diff = 2.5,
    p_diff = 0.012,
    fdr_diff = 0.02,
    control_mu_hat = 0.125,
    case_mu_hat = 0.275
  )
)

out <- plot_representative_samples(
  se_stats = se_stats,
  se_meta = se_meta,
  spe_list = spe_list,
  sig_col = "p_diff",
  alpha = 0.05,
  top_n = 1
)
names(out)

```

plot_spatial_network *Plot PANORAMIC spatial colocalization network*

Description

Wrapper to construct and visualize a PANORAMIC spatial colocalization network. It builds the directed network via `create_spatial_network()` and then renders it with `ggraph/tidygraph`.

Usage

```

plot_spatial_network(
  se_diff,
  fdr_threshold = 0.05,
  leiden_resolution = 1,

```

```

z_sign = c("both", "positive", "negative"),
include_nonsig = FALSE,
nonsig_max_fdr = 1,
directed = FALSE,
sig_operator = c("lt", "gt"),
layout = "fr",
node_size_by = "degree",
label_repel = TRUE,
label_box_padding = 0.2,
label_point_padding = 0.1,
label_force = 0.8,
return_net = FALSE
)

```

Arguments

se_diff A SummarizedExperiment returned by panoramic_meta_mv().

fdr_threshold Numeric threshold used for significance and edge classification.

leiden_resolution Numeric Leiden resolution passed to create_spatial_network().

z_sign Character sign filter for z_diff ("both", "positive", "negative").

include_nonsig Logical; include non-significant edges.

nonsig_max_fdr Numeric max FDR retained when include_nonsig = TRUE.

directed Logical; pass through to create_spatial_network().

sig_operator One of "lt" or "gt" passed through to create_spatial_network() for threshold direction.

layout Character string specifying the graph layout passed to ggraph (e.g. "fr", "kk", "stress"). Default "fr".

node_size_by Character name of a vertex attribute used to scale node sizes (e.g. "degree", "strength", "betweenness"). Default "degree".

label_repel Logical; if TRUE use repelled node labels.

label_box_padding Numeric box padding for repelled labels.

label_point_padding Numeric point padding for repelled labels.

label_force Numeric repulsion force for labels.

return_net Logical; if TRUE return a list with plot and net.

Value

A ggplot object by default, or a list with plot and net when return_net = TRUE.

Examples

```

se_diff <- SummarizedExperiment::SummarizedExperiment(
  assays = list(dummy = matrix(0, nrow = 3, ncol = 1)),
  rowData = S4Vectors::DataFrame(
    ct1 = c("A", "A", "B"),
    ct2 = c("B", "C", "C"),
    z_diff = c(2.0, -1.5, 1.2),

```

```

    p_diff = c(0.01, 0.03, 0.20),
    fdr_diff = c(0.02, 0.05, 0.30)
  )
)

if (requireNamespace("ggraph", quietly = TRUE) &&
    requireNamespace("tidygraph", quietly = TRUE)) {
  p_net <- plot_spatial_network(
    se_diff,
    fdr_threshold = 0.2,
    z_sign = "both",
    include_nonsig = TRUE,
    layout = "fr",
    node_size_by = "degree"
  )
  print(p_net)
}

```

plot_volcano

Volcano plot for differential spatial colocalization

Description

Updated volcano helper based on the CRC TMA manuscript workflow. It uses `beta_diff` for the x-axis and $-\log_{10}(p_diff)$ for the y-axis, and colors points by significance direction.

Usage

```

plot_volcano(
  se_diff,
  sig_col = c("fdr_diff", "p_diff"),
  alpha = 0.05,
  x_scale = c("beta_diff", "log2fc"),
  label_top = 12L,
  label_text_pt = 4,
  p_floor = 1e-300,
  title = NULL
)

```

Arguments

<code>se_diff</code>	A SummarizedExperiment with contrast columns in <code>rowData(se_diff)</code> (at least <code>ct1</code> , <code>ct2</code> , <code>beta_diff</code> , <code>p_diff</code> ; and <code>fdr_diff</code> when <code>sig_col = "fdr_diff"</code>).
<code>sig_col</code>	Character, one of <code>"fdr_diff"</code> or <code>"p_diff"</code> . Controls which column determines significance coloring.
<code>alpha</code>	Numeric threshold for significance based on <code>sig_col</code> .
<code>x_scale</code>	Character, one of <code>"beta_diff"</code> or <code>"log2fc"</code> . <code>"log2fc"</code> uses $\text{sign}(\text{beta_diff}) * \log_2(1 + \text{abs}(\text{beta_diff}))$.
<code>label_top</code>	Integer number of significant hits to label. Use <code>NULL</code> or <code>0</code> to disable labels.
<code>label_text_pt</code>	Numeric font size (points) for significant-hit labels.
<code>p_floor</code>	Numeric floor applied to <code>p_diff</code> before $-\log_{10}()$.
<code>title</code>	Optional character title.

Value

A ggplot object.

Examples

```
se_diff <- SummarizedExperiment::SummarizedExperiment(  
  assays = list(dummy = matrix(0, nrow = 2, ncol = 1)),  
  rowData = S4Vectors::DataFrame(  
    ct1 = c("A", "A"),  
    ct2 = c("B", "C"),  
    radius_um = c(10, 10),  
    beta_diff = c(0.4, -0.3),  
    p_diff = c(0.01, 0.20),  
    fdr_diff = c(0.02, 0.30)  
  )  
)  
m <- S4Vectors::metadata(se_diff)  
m$panoramic <- list(contrast = list(control = "control", case = "case"))  
S4Vectors::metadata(se_diff) <- m  
plot_volcano(se_diff, sig_col = "fdr_diff")
```

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