Package 'RPBC'

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Title Region-Preserving Batch Correction for Paired Region-Resolved Single-Cell Data

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Description Implements Region-Preserving Batch Correction (RPBC), an empirical-Bayes location-scale framework for paired region-resolved single-cell and spatial-omics data. RPBC preserves a patient-balanced population-average regional contrast while harmonizing patient-wide location shifts, patient-specific regional deviations, and patient-region scale heterogeneity. The package also provides Adaptive RPBC for group-size-dependent stabilization of patient-region scale variation and covariate-adjusted RPBC for preserving prespecified patient-level covariate-associated variation during harmonization. RPBC is designed to interoperate with Bioconductor data structures for single-cell and spatial experiments.

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`RPBC-package` *RPBC: Region-Preserving Batch Correction for Paired Region-Resolved Single-Cell Data*

Description

Implements Region-Preserving Batch Correction (RPBC), an empirical-Bayes location-scale framework for paired region-resolved single-cell and spatial-omics data. RPBC preserves a patient-balanced population-average regional contrast while harmonizing patient-wide location shifts, patient-specific regional deviations, and patient-region scale heterogeneity. The package also provides Adaptive RPBC for group-size-dependent stabilization of patient-region scale variation and covariate-adjusted RPBC for preserving prespecified patient-level covariate-associated variation during harmonization. RPBC is designed to interoperate with Bioconductor data structures for single-cell and spatial experiments.

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`haley_gbm_example` *Haley GBM IMC Example Dataset*

Description

A representative example dataset for demonstrating Region-Preserving Batch Correction (RPBC) using glioblastoma imaging mass cytometry (IMC) data. The dataset retains all seven patients and the paired Core/Edge design, with 30 cells sampled from each patient-region combination.

Usage

```
data(haley_gbm_example)
```

Format

A `SpatialExperiment` object with 10 markers (rows) and 420 cells (columns). The `"counts"` assay contains raw IMC intensities.

Cell-level metadata include:

cell_id Unique cell identifier.

ROI Region-of-interest identifier.

patient_id Patient identifier.

region_type Paired tumor region, coded as `"Core"` or `"Edge"`.

age Patient age.

sex Patient sex.

mgmt_status MGMT status.

Details

The dataset contains 10 representative biological markers measured across 420 cells. Raw IMC intensities are stored in the `"counts"` assay, allowing preprocessing transformations to be applied directly through `rpbc()`.

This example dataset was constructed by sampling 30 cells from each patient-region combination while retaining all seven patients and both Core and Edge regions. It is intended for package examples, testing, and vignettes and does not represent the complete Haley GBM IMC dataset.

The 10 included markers are CD45, CD3, Cd8a, CD68, CD163, GFAP, Sox2, Olig2, Ki67, and Vimentin.

Source

Haley MJ, et al. (2024). Hypoxia coordinates the spatial landscape of myeloid cells within glioblastoma to affect survival. *Science Advances*, 10(20), eadj3301. https://doi.org/10.1126/sciadv.adj3301

Haley M, Couper K. (2024). Imaging mass cytometry data from IDH wildtype glioblastomas. Dryad. https://doi.org/10.5061/dryad.2z34tmprw

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`rpbc` *Region-Preserving Batch Correction*

Description

Apply Region-Preserving Batch Correction (RPBC) to paired region-resolved single-cell or spatial data.

Usage

```
rpbc(
  object,
  patient,
  region,
  assay_name = "counts",
  transform = c("none", "asinh", "log1p"),
```

```
  cofactor = 5,
  covariates = NULL,
  adaptive = FALSE,
  output_assay = "rpbc",
  core_level = "Core",
  edge_level = "Edge",
  conv = 1e-04,
  max_iter = 100L,
  eps = 1e-08,
  delta_adaptive_k = 1,
  delta_bounds = c(0.5, 2),
  return_fit = FALSE
)
```

Arguments

object	A SingleCellExperiment or SpatialExperiment object.
patient	Character string naming the column in colData(object) containing patient identifiers.
region	Character string naming the column in colData(object) containing the paired region labels.
assay_name	Character string naming the assay to use as input. Default is "counts". For count-based sequencing data, an appropriately normalized and log-transformed assay such as "logcounts" (e.g., log2(CPM + 1)) may be supplied with transform = "none".
transform	Character string specifying the transformation applied to the selected assay before RPBC harmonization. One of "none", "asinh" or "log1p". Default is "none".
cofactor	Positive numeric value used when transform = "asinh". The transformation is asinh(x / cofactor). Default is 5.
covariates	Optional character vector naming patient-level covariates in colData(object). Covariates supplied at the cell level must be constant within patient. If NULL, ordinary RPBC is used.
adaptive	Logical. If TRUE, use Adaptive RPBC. Adaptive RPBC cannot currently be combined with covariate adjustment.
output_assay	Character string giving the name of the assay in which the harmonized expression matrix will be stored. Default is "rpbc".
core_level	Character string identifying the Core region.
edge_level	Character string identifying the Edge region.
conv	Positive convergence tolerance for empirical-Bayes estimation.
max_iter	Positive integer giving the maximum number of empirical-Bayes iterations.
eps	Small positive numerical constant used for numerical stability.
delta_adaptive_k	Positive Adaptive RPBC stabilization constant. The validated default is 1.
delta_bounds	Numeric vector of length two giving the lower and upper bounds for Adaptive RPBC patient-region variance multipliers. The validated default is c(0.5, 2.0).
return_fit	Logical. If FALSE, return the modified Bioconductor object. If TRUE, return a list containing both the modified object and the full internal RPBC fit.

Details

RPBC harmonizes patient and patient-by-region nuisance variation while preserving the prespecified population-average regional effect.

The function supports:

- ordinary RPBC;
- covariate-adjusted RPBC; and
- Adaptive RPBC.

Ordinary and covariate-adjusted RPBC use the same internal statistical engine. Adaptive RPBC uses a separate internal engine because its patient-region scale update includes group-size-dependent stabilization.

Value

By default, the input object with the harmonized expression matrix stored in `output_assay`. If `return_fit = TRUE`, a list containing `object` and `fit`.

Examples

```
data("haley_gbm_example", package = "RPBC")

# Ordinary RPBC
example_ordinary <- rpbc(
  object = haley_gbm_example,
  patient = "patient_id",
  region = "region_type",
  assay_name = "counts",
  transform = "asinh",
  cofactor = 5,
  adaptive = FALSE,
  output_assay = "rpbc"
)

# Adaptive RPBC
example_adaptive <- rpbc(
  object = haley_gbm_example,
  patient = "patient_id",
  region = "region_type",
  assay_name = "counts",
  transform = "asinh",
  cofactor = 5,
  adaptive = TRUE,
  output_assay = "rpbc_adaptive"
)

# Covariate-adjusted RPBC
example_covariate <- rpbc(
  object = haley_gbm_example,
  patient = "patient_id",
  region = "region_type",
  assay_name = "counts",
  transform = "asinh",
  cofactor = 5,
  covariates = c("age", "sex"),
```

```
  adaptive = FALSE,
  output_assay = "rpbc_covariate"
)
```

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