Package ‘harmony’

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Title Fast, Sensitive, and Accurate Integration of Single Cell Data

Version 0.1.0

Description Implementation of the Harmony algorithm for single cell integration, described in Kor-
sunskey et al <doi:10.1038/s41592-019-0619-0>. Package includes a standalone Harmony func-
tion and interfaces to external frameworks.

URL software.broadinstitute.org/harmony

License GPL-3

Encoding UTF-8

RoxygenNote 7.1.1

Depends R(>= 3.5.0), Rcpp

LazyData true

LinkingTo Rcpp, RcppArmadillo, RcppProgress

Imports dplyr, cowplot, tidyr, ggplot2, irlba, Matrix, methods, tibble, rlang

Suggests Seurat, testthat, knitr, rmarkdown

VignetteBuilder knitr

NeedsCompilation yes

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#### cell_lines

**Description**

List of metadata table and scaled PCs matrix

**Usage**

`cell_lines`

**Format**

- `meta_data`: data.table of 9478 rows with defining dataset and cell_type
- `scaled_pcs`: data.table of 9478 rows (cells) and 20 columns (PCs)

**Source**

https://support.10xgenomics.com/single-cell-gene-expression/datasets

#### cell_lines_small

**Description**

Same as `cell_lines` but smaller (300 cells).

**Usage**

`cell_lines_small`

**Format**

An object of class `list` of length 2.

**Source**

https://support.10xgenomics.com/single-cell-gene-expression/datasets
Harmony: fast, accurate, and robust single cell integration.

Description
Algorithm for single cell integration.

Usage
1. `HarmonyMatrix` to run Harmony on gene expression or PCA embeddings matrix.
2. `RunHarmony` to run Harmony on Seurat objects.

Useful links
2. Read the manuscript online.

HarmonyMatrix
Main Harmony interface

Description
Use this to run the Harmony algorithm on gene expression or PCA matrix.

Usage

```r
HarmonyMatrix(
  data_mat,
  meta_data,
  vars_use,
  do_pca = TRUE,
 npcs = 20,
  theta = NULL,
  lambda = NULL,
  sigma = 0.1,
  nclust = NULL,
  tau = 0,
  block.size = 0.05,
  max.iter.harmony = 10,
  max.iter.cluster = 200,
  epsilon.cluster = 1e-05,
  epsilon.harmony = 1e-04,
  plot_convergence = FALSE,
  return_object = FALSE,
  verbose = TRUE,
)```

```
```r
reference_values = NULL,
cluster_prior = NULL
)

Arguments

data_mat Matrix of normalized gene expression (default) or PCA embeddings (see do_pca). Cells can be rows or columns.

meta_data Either (1) Dataframe with variables to integrate or (2) vector with labels.

vars_use If meta_data is dataframe, this defined which variable(s) to remove (character vector).

do_pca Whether to perform PCA on input matrix.
npcs If doing PCA on input matrix, number of PCs to compute.

theta Diversity clustering penalty parameter. Specify for each variable in vars_use. Default theta=2. theta=0 does not encourage any diversity. Larger values of theta result in more diverse clusters.

lambda Ridge regression penalty parameter. Specify for each variable in vars_use. Default lambda=1. Lambda must be strictly positive. Smaller values result in more aggressive correction.

sigma Width of soft kmeans clusters. Default sigma=0.1. Sigma scales the distance from a cell to cluster centroids. Larger values of sigma result in cells assigned to more clusters. Smaller values of sigma make soft kmeans cluster approach hard clustering.

nclust Number of clusters in model. nclust=1 equivalent to simple linear regression.

tau Protection against overclustering small datasets with large ones. tau is the expected number of cells per cluster.

block.size What proportion of cells to update during clustering. Between 0 to 1, default 0.05. Larger values may be faster but less accurate.

max.iter.harmony Maximum number of rounds to run Harmony. One round of Harmony involves one clustering and one correction step.

max.iter.cluster Maximum number of rounds to run clustering at each round of Harmony.

epsilon.cluster Convergence tolerance for clustering round of Harmony. Set to -Inf to never stop early.

epsilon.harmony Convergence tolerance for Harmony. Set to -Inf to never stop early.

plot_convergence Whether to print the convergence plot of the clustering objective function. TRUE to plot, FALSE to suppress. This can be useful for debugging.

return_object (Advanced Usage) Whether to return the Harmony object or only the corrected PCA embeddings.

verbose Whether to print progress messages. TRUE to print, FALSE to suppress.
```
moeb_get_betas

reference_values
(Advanced Usage) Defines reference dataset(s). Cells that have batch variables values matching reference_values will not be moved.

cluster_prior 
(Advanced Usage) Provides user defined clusters for cluster initialization. If the number of provided clusters C is less than K, Harmony will initialize K-C clusters with kmeans. C cannot exceed K.

Value
By default, matrix with corrected PCA embeddings. If return_object is TRUE, returns the full Harmony object (R6 reference class type).

Examples

## By default, Harmony inputs a normalized gene expression matrix
## Not run:
harmony_embeddings <- HarmonyMatrix(exprs_matrix, meta_data, 'dataset')

## End(Not run)

## Harmony can also take a PCA embeddings matrix
data(cell_lines_small)
pca_matrix <- cell_lines_small$scaled_pcs
meta_data <- cell_lines_small$meta_data
harmony_embeddings <- HarmonyMatrix(pca_matrix, meta_data, 'dataset', do_pca=FALSE)

## Output is a matrix of corrected PC embeddings
dim(harmony_embeddings)
harmony_embeddings[seq_len(5), seq_len(5)]

## Finally, we can return an object with all the underlying data structures
harmony_object <- HarmonyMatrix(pca_matrix, meta_data, 'dataset', do_pca=FALSE, return_object=TRUE)
dim(harmony_object$Y) # cluster centroids
dim(harmony_object$R) # soft cluster assignment
dim(harmony_object$Z_corr) # corrected PCA embeddings
head(harmony_object$O) # batch by cluster co-occurrence matrix

moe_ridge_get_betas Get beta Utility

Description
Utility function to get ridge regression coefficients from trained Harmony object
Usage

moe_ridge_get_betas(harmonyObj)

Arguments

harmonyObj  Trained harmony object. Get this by running HarmonyMatrix function with return_object=TRUE.

Value

Returns nothing, modifies object in place.

Description

Run Harmony algorithm with Seurat and SingleCellAnalysis pipelines.

Usage

RunHarmony(object, group.by.vars, ...)

## S3 method for class 'Seurat'
RunHarmony(
  object,
  group.by.vars,
  reduction = "pca",
  dims.use = NULL,
  theta = NULL,
  lambda = NULL,
  sigma = 0.1,
  nclust = NULL,
  tau = 0,
  block.size = 0.05,
  max.iter.harmony = 10,
  max.iter.cluster = 20,
  epsilon.cluster = 1e-05,
  epsilon.harmony = 1e-04,
  plot_convergence = FALSE,
  verbose = TRUE,
  reference_values = NULL,
  reduction.save = "harmony",
  assay.use = "RNA",
  project.dim = TRUE,
  ...
)

)
RunHarmony

Arguments

object
Pipeline object. Must have PCA computed.

group.by.vars
Which variable(s) to remove (character vector).
...
other parameters
reduction
Name of dimension reduction to use. Default is PCA.
dims.use
Which PCA dimensions to use for Harmony. By default, use all
theta
Diversity clustering penalty parameter. Specify for each variable in group.by.vars. Default theta=2. theta=0 does not encourage any diversity. Larger values of theta result in more diverse clusters.
lambda
Ridge regression penalty parameter. Specify for each variable in group.by.vars. Default lambda=1. Lambda must be strictly positive. Smaller values result in more aggressive correction.
sigma
Width of soft kmeans clusters. Default sigma=0.1. Sigma scales the distance from a cell to cluster centroids. Larger values of sigma result in cells assigned to more clusters. Smaller values of sigma make soft kmeans cluster approach hard clustering.
nclust
Number of clusters in model. nclust=1 equivalent to simple linear regression.
tau
Protection against overclustering small datasets with large ones. tau is the expected number of cells per cluster.
block.size
What proportion of cells to update during clustering. Between 0 to 1, default 0.05. Larger values may be faster but less accurate
max.iter.harmony
Maximum number of rounds to run Harmony. One round of Harmony involves one clustering and one correction step.
max.iter.cluster
Maximum number of rounds to run clustering at each round of Harmony.
epsilon.cluster
Convergence tolerance for clustering round of Harmony. Set to -Inf to never stop early.
epsilon.harmony
Convergence tolerance for Harmony. Set to -Inf to never stop early.
plot_convergence
Whether to print the convergence plot of the clustering objective function. TRUE to plot, FALSE to suppress. This can be useful for debugging.
verbose
Whether to print progress messages. TRUE to print, FALSE to suppress.
reference_values
(Advanced Usage) Defines reference dataset(s). Cells that have batch variables values matching reference_values will not be moved
reduction.save
Keyword to save Harmony reduction. Useful if you want to try Harmony with multiple parameters and save them as e.g. 'harmony_theta0', 'harmony_theta1', 'harmony_theta2'
assay.use
(Seurat V3 only) Which assay to Harmonize with (RNA by default).
project.dim
Project dimension reduction loadings. Default TRUE.
Value

Seurat (version 3) object. Harmony dimensions placed into dimensional reduction object harmony. For downstream Seurat analyses, use reduction='harmony'.
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