Package 'harmony'

November 14, 2022

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

Version 0.1.1

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

URL software.broadinstitute.org/harmony

License GPL-3

Encoding UTF-8

RoxygenNote 7.2.1

Depends R(>= 3.4.0), Rcpp

LazyData true

LinkingTo Rcpp, RcppArmadillo, RcppProgress

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

Suggests SingleCellExperiment, Seurat (>= 4.1.1), testthat, knitr, rmarkdown

VignetteBuilder knitr

NeedsCompilation yes

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R topics documented:

`cell_lines` *List of metadata table and scaled PCs matrix*

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://www.10xgenomics.com

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

Description

Same as cell_lines but smaller (300 cells).

Usage

```
cell_lines_small
```

Format

An object of class `list` of length 2.

Source

https://www.10xgenomics.com

harmony *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 or SingleCellExperiment objects.

Useful links

1. Report bugs at https://github.com/immunogenomics/harmony/issues
2. Read the manuscript online.

HarmonyMatrix *Main Harmony interface*

Description

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

Usage

```
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,
```

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

Arguments

data_mat	Matrix of normalized gene expession (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.

`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-occurence 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.

RunHarmony *Harmony single cell integration*

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 = NULL,
  project.dim = TRUE,
  ...
)
```

```
## S3 method for class 'SingleCellExperiment'
RunHarmony(
  object,
  group.by.vars,
  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",
  ...
)
```

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 run PCA on if no PCA present?

`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'.

SingleCellExperiment object. After running RunHarmony, the corrected cell embeddings can be accessed with reducedDim(object, "Harmony").

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