Package: hicream (via r-universe)

June 5, 2026

Title HIC diffeREntial Analysis Method

Version 0.0.4

Date 2026-01-30

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Description Perform Hi-C data differential analysis based on pixel-level differential analysis and a post hoc inference strategy to quantify signal in clusters of pixels. Clusters of pixels are obtained through a connectivity-constrained two-dimensional hierarchical clustering.

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URL `https://scales.pages-forge.inrae.fr/hicream/`, `https://forge.inrae.fr/scales/hicream`

BugReports `https://forge.inrae.fr/scales/hicream/-/issues`

Depends R (>= 4.0.0), reticulate

SystemRequirements Python (>= 3.9)

Imports adjclust, auk, BiocGenerics, csaw, diffHic, dplyr, edgeR, GenomeInfoDb, GenomicRanges, InteractionSet, limma, Matrix, methods, reshape2, rlang, S4Vectors, stats, SummarizedExperiment, utils, viridis

Suggests knitr, rmarkdown

Encoding UTF-8

RoxygenNote 7.3.3

VignetteBuilder knitr

NeedsCompilation no

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Config/pak/sysreqs make libbz2-dev libicu-dev liblzma-dev libpng-dev libxml2-dev libssl-dev python3 libx11-dev xz-utils zlib1g-dev

Repository https://eoojj.r-universe.dev

Date/Publication 2026-01-30 15:50:02 UTC

RemoteUrl https://github.com/cran/hicream

RemoteRef HEAD

RemoteSha b003479e57030d3007e897943556f668cf536fc5

Contents

`AggloClust2D` *Perform Constrained 2D Agglomerative Clustering*

Description

This function performs a connectivity constrained 2D agglomerative clustering using `scikit-learn` function `AgglomerativeClustering` and outputs an object of class `hclust` that stores the hierarchy of merges and value of criterion at each merge. It also outputs the optimal level of the hierarchy with respect to the elbow heuristic.

Usage

```
AggloClust2D(counts, nbClust = NULL)

## S3 method for class 'res2D'
print(x, ...)

## S3 method for class 'res2D'
summary(object, ...)

## S3 method for class 'res2D'
plot(x, ...)
```

Arguments

`counts`	an object of class `InteractionSet` obtained from the function `loadData` or an object of class `resdiff` obtained from function `performTest`.
`nbClust`	integer. Number of clusters to obtain. Set to `NULL` by default.
`x`	a `res2D` object to plot
`...`	not used
`object`	a `res2D` object to summarize

Value

An object of class `res2D` containing:

`tree`	an object of class `hclust`
`nbClust`	the number of clusters corresponding either to the value passed by the user or to the optimal level of clusters as provided by the elbow heuristic
`clustering`	obtained clustering

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Examples

```
data("pighic")

res2D <- AggloClust2D(pighic$data)
if (!is.null(res2D)) { # in case Python or modules are not available
  clusters <- res2D$clustering
  print(res2D)
  summary(res2D)
  plot(res2D)
}
```

`loadData` *Load and Normalize Hi-C Data*

Description

This function loads data necessary for the analysis and outputs them in a suitable format for `performTest` and `2Dclust`.

Usage

```
loadData(files, index, chromosome, normalize = TRUE)
```

Arguments

`files`	character vector. Paths to Hi-C matrices in bed format.
`index`	character. A path to an index file in bed format.
`chromosome`	character or integer. Chromosome to select.
`normalize`	logical. Whether or not to normalize the output (with MA method). Set to `TRUE` by default.

Value

An `InteractionSet` corresponding to all interactions present in at least one of the input matrices and corresponding counts across all matrices.

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Examples

```
replicates <- 1:2
cond <- "90"
allBegins <- interaction(expand.grid(replicates, cond), sep = "-")
allBegins <- as.character(allBegins)
chromosome <- 1
nbChr <- 1
allMat <- sapply(allBegins, function(ab) {
  matFile <- paste0("Rep", ab, "-chr", chromosome, "_200000.bed")
  })
index <- system.file("extdata", "index.200000.longest18chr.abs.bed",
                    package = "hicream")
                    format <- rep("HiC-Pro", length(replicates) * length(cond) * nbChr)
binsize <- 200000
files <- system.file("extdata", unlist(allMat), package = "hicream")
exData <- loadData(files, index, chromosome, normalize = TRUE)
```

`performTest` *Perform diffHic Test*

Description

This function performs diffHic differential analysis for every pixel of the matrix.

Usage

```
performTest(
  matrices,
  cond,
  outFile = NULL,
  filterLc = FALSE,
  filterFlank = FALSE,
  flank = NULL
)

## S3 method for class 'resdiff'
print(x, ...)

## S3 method for class 'resdiff'
summary(object, ...)

## S3 method for class 'resdiff'
plot(x, whichPlot = c("p.value", "p.adj", "logFC"), ...)
```

Arguments

`matrices`	an object of class `InteractionSet` obtained from the function `loadData`. Conditions correspond to the columns (one column per replicate).
`cond`	a vector indicating the condition of each column of `matrices`.
`outFile`	path to export outputs of the function, set to `NULL` by default, in which case results are not exported.
`filterLc`	logical. Whether to filter out low counts or not. Set to `FALSE` by default, in which case no filtering is performed. See `filterTrended` for more details.
`filterFlank`	logical. Whether to filter out on enriched pairs. Set to `FALSE` by default, in which case no filtering is performed. See `enrichedPairs` and `filterPeaks` for more details.
`flank`	flank parameter used only if `filterFlank = TRUE`. Set to `NULL` by default. See `enrichedPairs` for more details.
`x`	a `resdiff` object to plot
`...`	not used
`object`	a `resdiff` object to print
`whichPlot`	a character string indicating which plot to display. Possible values are `"p.value"`, `"p.adj"` and `"logFC"`. Set to `"p.value"` by default.

Value

An object of class `resdiff` with the following entries:

`region1`	the first bin of the interaction
`region2`	the second bin of the interaction
`p.value`	the p-value of the `diffHic` test
`p.adj`	the adjusted p-value of the `diffHic` test
`logFC`	the log2-fold-change of the interaction

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Examples

```
data("pighic")
resdiff <- performTest(pighic$data, pighic$conditions)
resdiff
summary(resdiff)
plot(resdiff)
plot(resdiff, whichPlot = "p.adj")
plot(resdiff, whichPlot = "logFC")
```

`pighic` *Dataset "pighic"*

Description

6 Hi-C matrices (3 in each condition) obtained from two different developmental stages of pig embryos (90 and 110 days of gestation) corresponding to chromosome 1.

Format

An object with two entries:

data an object of class `InteractionSet` containing 6 Hi-C matrices from 2 conditions (3 each) for 21 interactions.

conditions a two-level factor indicating the condition of each matrix in `data`.

Details

The data are identical to the dataset present in the package `treediff`.

References

Nathalie Vialaneix, Gwendaelle Cardenas, Marie Chavent, Sylvain Foissac, Pierre Neuvial, and Nathanael Randriamihamison (2023). treediff: Testing Differences Between Families of Trees. https://cran.r-project.org/package=treediff

Examples

```
data(pighic)
```

`postHoc` *Perform Post Hoc Inference*

Description

This function performs post-hoc inference on all provided clusters using `performTest` results.

Usage

```
postHoc(resdiff, clusters, alpha, fill = FALSE, stepDown = TRUE)

## S3 method for class 'resposthoc'
print(x, ...)

## S3 method for class 'resposthoc'
summary(object, ...)

## S3 method for class 'resposthoc'
plot(x, ...)
```

Arguments

`resdiff`	An object of class `resdiff` obtained from the function `performTest`.
`clusters`	A vector corresponding to a clustering of resdiff rows.
`alpha`	A number between 0 and 1 at which the computed post hoc bounds will be valid.
`fill`	A boolean value. If TRUE (the default), enforce the total number of tests to be $p*(p+1)/2$ by adding ones to the p-value vector for non tested entries.
`stepDown`	A boolean value. If FALSE, the single step Simes method is used. If TRUE (the default), the step-down Simes method is used. The latter is more powerful when the signal is strong.
`x`	a `resposthoc` object to plot
`...`	not used
`object`	a `resposthoc` object to summarize

Value

An object of class `resposthoc` containing a matrix with true positive proportions for each interaction and a dataframe with the following entries:

`region1`	The first bin of the interaction.
`region2`	The second bin of the interaction.
`clust`	The cluster the interaction belongs to.
`TDP`	The minimal post hoc true discovery (positive) proportion of the cluster the interaction belongs to.
`p.value`	The p-value of the diffHic test.
`p.adj`	The adjusted p-value of the diffHic test.
`logFC`	The log2-fold-change of the interaction.
`meanlogFC`	The mean of the log2-fold-change for the cluster the interaction belongs to.
`varlogFC`	The variance of the log2-fold-change for the cluster the interaction belongs to.
`propPoslogFC`	The proportion of interactions with positive log2-fold-change in the cluster the interaction belongs to.

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Examples

```
data("pighic")
resdiff <- performTest(pighic$data, pighic$conditions)
res2D <- AggloClust2D(pighic$data)
if (!is.null(res2D)) { # in case Python or modules are not available
  clusters <- res2D$clustering
  alpha <- 0.05
  resposthoc <- postHoc(resdiff, clusters, alpha)
  resposthoc
  summary(resposthoc)
  plot(resposthoc)
}
```

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