# Package 'EpiCompare'

November 28, 2024

Type Package

Title Comparison, Benchmarking & QC of Epigenomic Datasets

Version 1.10.0

**Description** EpiCompare is used to compare and analyse epigenetic datasets for quality control and benchmarking purposes.

The package outputs an HTML report consisting of three sections:

- (1. General metrics) Metrics on peaks (percentage of blacklisted and non-standard peaks, and peak widths) and fragments (duplication rate) of samples,
- (2. Peak overlap) Percentage and statistical significance of overlapping and non-overlapping peaks. Also includes upset plot and (3. Functional annotation) functional annotation (ChromHMM, ChIPseeker and enrichment analysis) of peaks.

Also includes peak enrichment around TSS.

License GPL-3

URL https://github.com/neurogenomics/EpiCompare

BugReports https://github.com/neurogenomics/EpiCompare/issues

**Depends** R (>= 4.2.0)

**Imports** AnnotationHub, ChIPseeker, data.table, genomation, GenomicRanges, IRanges, GenomeInfoDb, ggplot2 (>= 3.5.0), htmltools, methods, plotly, reshape2, rmarkdown, rtracklayer, stats, stringr, utils, BiocGenerics, downloadthis, parallel

Suggests rworkflows, BiocFileCache, BiocParallel, BiocStyle,

clusterProfiler, GenomicAlignments, grDevices, knitr,

org.Hs.eg.db, testthat ( $\geq 3.0.0$ ), tidyr,

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TxDb.Hsapiens.UCSC.hg38.knownGene,

TxDb.Mmusculus.UCSC.mm9.knownGene,

TxDb.Mmusculus.UCSC.mm10.knownGene,

BSgenome. Hsapiens. UCSC.hg19, BSgenome. Hsapiens. UCSC.hg38,

BSgenome.Mmusculus.UCSC.mm9, BSgenome.Mmusculus.UCSC.mm10,

ComplexUpset, plyranges, scales, Matrix, consensusSeekeR, heatmaply, viridis

VignetteBuilder knitr

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# Description

Convert a ggplot object to plotly, and enable it to be plotted within an Rmarkdown HTML file.

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#### Usage

```
as_interactive(
  plt,
  to_widget = isTRUE(getOption("knitr.in.progress")),
  add_boxmode = FALSE
)
```

#### **Arguments**

plt ggplot object.

to\_widget Convert to a widget so it works within Rmarkdown HTML files. By default, this

will be only be set to TRUE when being run within the context of knitr rendering.

add\_boxmode Add extra layout to enable dodged boxplots.

#### Value

A plotly object or a tagList wrapping the plotly object.

### Source

GitHub Issue to check whether knitting

bpplapply

Wrapper for bplapply

### **Description**

Wrapper function for bplapply that automatically handles issues with **BiocParallel** related to different OS platforms.

### Usage

```
bpplapply(
    X,
    FUN,
    apply_fun = parallel::mclapply,
    workers = check_workers(),
    progressbar = workers > 1,
    verbose = workers == 1,
    use_snowparam = TRUE,
    register_now = FALSE,
    ...
)
```

### Arguments

X Any object for which methods length, [, and [[ are implemented.

FUN The function to be applied to each element of X.

apply\_fun Iterator function to use.

workers Number of threads to parallelize across.

checkCache 5

progressbar logical(1) Enable progress bar (based on plyr:::progress\_text).

verbose Print messages.

use\_snowparam Whether to use SnowParam (default: TRUE) or MulticoreParam (FALSE) when

parallelising across multiple workers.

register\_now Register the cores now with register (TRUE), or simply return the BPPARAM object

(default: FALSE).

... Arguments passed on to BiocParallel::bplapply

BPPARAM An optional BiocParallelParam instance determining the parallel back-end to be used during evaluation, or a list of BiocParallelParam instances, to be applied in sequence for nested calls to **BiocParallel** functions.

BPREDO A list of output from bplapply with one or more failed elements. When a list is given in BPREDO, bpok is used to identify errors, tasks are rerun and inserted into the original results.

BPOPTIONS Additional options to control the behavior of the parallel evaluation, see bpoptions.

#### Value

(Named) list.

### **Examples**

```
X <- stats::setNames(seq_len(length(letters)), letters)
out <- bpplapply(X, print)</pre>
```

checkCache

Check cache

### **Description**

Quick function to check if object is already saved.

#### Usage

```
checkCache(cache = BiocFileCache::BiocFileCache(ask = FALSE), url)
```

### **Arguments**

cache BiocFileCache.
url Path to cached file.

# Value

path

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check\_cell\_lines

Check cell lines

### **Description**

Check whether a list of cell lines matches any of those that are made available through EpiCompare.

# Usage

```
check_cell_lines(cell_lines = NULL, verbose = TRUE)
```

# Arguments

cell\_lines A character vector of cell line names. If NULL (default), will return names of all

cell lines.

verbose Print messages.

### Value

Character vector, or NULL.

check\_genome\_build

Check genome build

# Description

Check that the genome build is valid and require specific reference datasets to be installed.

# Usage

```
check_genome_build(genome_build, type = "txdb")
```

# Arguments

genome\_build Genome build name.

type whether to fetch the txdb or bsgen reference data

### Value

txdb or bsgen

check\_grlist\_cols 7

check\_grlist\_cols

Check GRanges list columns

# Description

Check that at least one of the required columns is in a list of GRanges objects. Elements that do not meet this criterion will be dropped from the list.

# Usage

```
check_grlist_cols(grlist, target_cols)
```

# **Arguments**

grlist Named list of GRanges objects.

target\_cols A character vector of column names to search for.

### Value

Named list of GRanges objects.

check\_list\_names

Check peaklist is named

### **Description**

This function checks whether the peaklist is named. If not, default file names are assigned.

### Usage

```
check_list_names(peaklist, default_prefix = "sample")
```

# Arguments

```
peaklist A list of peak files as GRanges object.
```

default\_prefix Default prefix to use when creating names for peaklist.

### Value

named peaklist

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check\_workers

Check workers

# Description

Assign parallel worker cores.

#### Usage

```
check_workers(workers = NULL)
```

### **Arguments**

workers

Number of cores to parallelise across (in applicable functions). If NULL, will set to the total number of available cores minus 1.

### Value

Integer

### **Examples**

```
workers <- check_workers()</pre>
```

clean\_granges

Clean GRanges

# Description

Remove columns from the metadata (GenomicRanges::mcols) that conflicts with GRanges conventions.

# Usage

```
clean_granges(
   gr,
nono_cols = c("seqnames", "ranges", "strand", "seqlevels", "seqlengths", "isCircular",
        "start", "end", "width", "element")
)
```

### **Arguments**

gr A GRanges object.

nono\_cols Problematic columns to search for and remove (if present).

# Value

Cleaned GRanges object.

CnR\_H3K27ac 9

CnR\_H3K27ac

Example CUT&Run peak file

#### **Description**

Human H3K27ac peak file generated with CUT&Run using K562 cell-line from Meers et al., (2019). Human genome build hg19 was used. Raw peak file (.BED) was obtained from GEO (https://trace.ncbi.nlm.nih.gov/Traces/sra/?run=SRR8581604). Peak calling was performed by Leyla Abbasova using MACS2. The peak file was then processed into GRanges object. Peaks located on chromosome 1 were subsetted to reduce the dataset size.

#### Usage

```
data("CnR_H3K27ac")
```

#### **Format**

An object of class GRanges of length 2707.

#### **Source**

The code to prepare the .Rda file from the raw peak file is:

usethis::use\_data(CnR\_H3K27ac, overwrite = TRUE)

```
# sequences were directly downloaded from https://trace.ncbi.nlm.nih.gov/Traces/sra/?run=SRR8581604
# and peaks (BED file) were generated by Leyla Abbasova (Neurogenomics Lab, Imperial College
London)
CnR_H3K27ac <- ChIPseeker::readPeakFile("path", as = "GRanges")
CnR_H3K27ac <- CnR_H3K27ac[seqnames(CnR_H3K27ac)== "chr1"]
my_label <-c("name", "score", "strand", "signalValue", "pValue", "qValue", "peak")
colnames(GenomicRanges::mcols(CnR_H3K27ac)) <- my_label</pre>
```

CnR\_H3K27ac\_picard

Example Picard duplication metrics file 2

#### **Description**

Duplication metrics output on CUT&Run H3K27ac file (sample accession: SRR8581604). Raw sequences were aligned to hg19 genome and after, Picard was performed by Leyla Abbasova. The duplication summary output generated by Picard was processed to reduce the size of data.

### Usage

```
data("CnR_H3K27ac_picard")
```

### Format

An object of class data. frame with 1 rows and 10 columns.

#### Source

```
The code to prepare the .Rda file is:
```

```
picard <- read.table("path/to/picard/duplication/output",header = TRUE, fill = TRUE)
CnR_H3K27ac_picard <- picard[1,]
usethis::use_data(CnR_H3K27ac_picard, overwrite = TRUE)</pre>
```

CnT H3K27ac

Example CUT&Tag peak file

#### **Description**

Human H3K27ac peak file generated with CUT&Tag using K562 cell-line from Kaya-Okur et al., (2019). Human genome build hg19 was used. Raw peak file (.BED) was obtained from GEO (https://trace.ncbi.nlm.nih.gov/Traces/sra/?run=SRR8383507). Peak calling was performed by Leyla Abbasova using MACS2. The peak file was then imported as an GRanges object. Peaks located on chromosome 1 were subsetted to reduce the dataset size.

#### Usage

```
data("CnT_H3K27ac")
```

#### **Format**

An object of class GRanges of length 1670.

#### Source

The code to prepare the .Rda file from the raw peak file is:

colnames(GenomicRanges::mcols(CnT\_H3K27ac)) <- my\_label</pre>

```
# sequences were directly downloaded from https://trace.ncbi.nlm.nih.gov/Traces/sra/?run=SRR8383507
# and peaks (BED file) were generated by Leyla Abbasova (Neurogenomics Lab, Imperial College
London)
CnT_H3K27ac <- ChIPseeker::readPeakFile("path", as = "GRanges")
CnT_H3K27ac <- CnT_H3K27ac[seqnames(CnT_H3K27ac)== "chr1"]
my_label <-c("name", "score", "strand", "signalValue", "pValue", "qValue", "peak")</pre>
```

usethis::use\_data(CnT\_H3K27ac)

CnT\_H3K27ac\_picard

Example Picard duplication metrics file 1

# Description

Duplication metrics output of CUT&Tag H3K27ac file (sample accession: SRR8581604). Raw sequences were aligned to hg19 genome and Picard was performed by Leyla Abbasova. The duplication summary output generated by Picard was processed to reduce the size of data.

#### Usage

```
data("CnT_H3K27ac_picard")
```

#### **Format**

An object of class data. frame with 1 rows and 10 columns.

#### **Source**

```
The code to prepare the .Rda file is:

picard <- read.table("path/to/picard/duplication/output",header = TRUE, fill = TRUE)]
CnT_H3K27ac_picard <- picard[1,]
usethis::use_data(CnT_H3K27ac_picard, overwrite = TRUE)
```

compute\_consensus\_peaks

Compute consensus peaks

### **Description**

Compute consensus peaks from a list of GRanges.

### Usage

```
compute_consensus_peaks(
  grlist,
  groups = NULL,
  genome_build,
  lower = 2,
  upper = Inf,
  min.gapwidth = 1L,
  method = c("granges", "consensusseeker"),
  ...
)
```

### **Arguments**

grlist Named list of GRanges objects.

groups A character vector of the same length as grlist defining how to group GRanges

objects when computing consensus peaks.

genome\_build Genome build name.

lower, upper The lower and upper bounds for the slice.

min.gapwidth Ranges separated by a gap of at least min.gapwidth positions are not merged.

method Method to call peaks with:

- "granges": Simple overlap procedure using GRanges functions. Faster but less accurate.
- "consensusseeker": Uses findConsensusPeakRegions to compute consensus peaks. Slower but more accurate.

### ... Arguments passed on to consensusSeekeR::findConsensusPeakRegions

- narrowPeaks a GRanges containing called peak regions of signal enrichment based on pooled, normalized data for all analyzed experiments. All GRanges entries must have a metadata field called "name" which identifies the region to the called peak. All GRanges entries must also have a row name which identifies the experiment of origin. Each peaks entry must have an associated narrowPeaks entry. A GRanges entry is associated to a narrowPeaks entry by having a identical metadata "name" field and a identical row name.
- peaks a GRanges containing called peaks of signal enrichment based on pooled, normalized data for all analyzed experiments. All GRanges entries must have a metadata field called "name" which identifies the called peak. All GRanges entries must have a row name which identifies the experiment of origin. Each peaks entry must have an associated narrowPeaks entry. A GRanges entry is associated to a narrowPeaks entry by having a identical metadata "name" field and a identical row name.
- chrInfo a Seqinfo containing the name and the length of the chromosomes to analyze. Only the chomosomes contained in this Seqinfo will be analyzed.
- extendingSize a numeric value indicating the size of padding on both sides of the position of the peaks median to create the consensus region. The minimum size of the consensus region is equal to twice the value of the extendingSize parameter. The size of the extendingSize must be a positive integer. Default = 250.
- expandToFitPeakRegion a logical indicating if the region size, which is set by the extendingSize parameter is extended to include the entire narrow peak regions of all peaks included in the unextended consensus region. The narrow peak regions of the peaks added because of the extension are not considered for the extension. Default: FALSE.
- shrinkToFitPeakRegion a logical indicating if the region size, which is set by the extendingSize parameter is shrinked to fit the narrow peak regions of the peaks when all those regions are smaller than the consensus region. Default: FALSE.
- minNbrExp a positive numeric or a positive integer indicating the minimum number of experiments in which at least one peak must be present for a potential consensus region. The numeric must be a positive integer inferior or equal to the number of experiments present in the narrowPeaks and peaks parameters. Default = 1.
- nbrThreads a numeric or a integer indicating the number of threads to use in parallel. The nbrThreads must be a positive integer. Default = 1.

#### **Details**

*NOTE:* If you get the error "Error in serialize(data, node\$con): error writing to connection", try running closeAllConnections and rerun compute\_consensus\_peaks. This error can sometimes occur when compute\_consensus\_peaks has been disrupted partway through.

#### Value

Named list of consensus peak GRanges.

#### Source

GenomicRanges tutorial

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#### consensusSeekeR

#### **Examples**

compute\_corr

Compute correlation matrix

#### **Description**

Compute correlation matrix on all peak files.

### Usage

```
compute_corr(
  peakfiles,
  reference = NULL,
  genome_build,
  keep_chr = NULL,
  drop_empty_chr = FALSE,
  bin_size = 5000,
  method = "spearman",
  intensity_cols = c("total_signal", "qValue", "Peak Score", "score"),
  return_bins = FALSE,
  fill_diag = NA,
  workers = check_workers(),
  save_path = tempfile(fileext = ".corr.csv.gz")
)
```

#### Arguments

peakfiles

A list of peak files as GRanges object and/or as paths to BED files. If paths are provided, EpiCompare imports the file as GRanges object. EpiCompare also accepts a list containing a mix of GRanges objects and paths. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If no names are specified, default file names will be assigned.

reference

A named list containing reference peak file(s) as GRanges object. Please ensure that the reference file is listed and named i.e. list("reference\_name" = reference\_peak). If more than one reference is specified, individual reports for each reference will be generated. However, please note that specifying more than one reference can take awhile. If a reference is specified, it enables two analyses: (1) plot showing statistical significance of overlapping/non-overlapping peaks; and (2) ChromHMM of overlapping/non-overlapping peaks.

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genome\_build The build of \*\*all\*\* peak and reference files to calculate the correlation matrix on. If all peak and reference files are not of the same build use liftover grlist

to convert them all before running. Genome build should be one of hg19, hg38,

mm9, mm10.

keep\_chr Which chromosomes to keep.

drop\_empty\_chr Drop chromosomes that are not present in any of the peakfiles (default: FALSE).

bin\_size Default of 100. Base-pair size of the bins created to measure correlation. Use

smaller value for higher resolution but longer run time and larger memory usage.

method Default spearman (i.e. non-parametric). A character string indicating which

correlation coefficient (or covariance) is to be computed. One of "pearson",

"kendall", or "spearman": can be abbreviated.

intensity\_cols Depending on which columns are present, this value will be used to get quantiles and ultimately calculate the correlations:

• "total\_signal": Used by the peak calling software SEACR. NOTE: Another SEACR column (e.g. "max\_signal") can be used together or instead of "total\_signal".

- "qValue"Used by the peak calling software MACS2/3. Should contain the negative log of the p-values after multiple testing correction.
- "Peak Score": Used by the peak calling software HOMER.

return\_bins If TRUE, returns a named list with both the rebinned (standardised) peaks ("bin")

and the correlation matrix ("cor"). If FALSE (default), returns only the correlation

matrix (unlisted).

fill\_diag Fill the diagonal of the overlap matrix.

workers Number of threads to parallelize across.

save\_path Path to save a table of correlation results to.

#### Value

correlation matrix

#### **Examples**

download\_button 15

#### **Description**

Save an object as RDS and create a download button that can be rendered to Rmarkdown HTML pages. Uses the package **downloadthis**.

#### Usage

```
download_button(
  object,
  save_output = FALSE,
  outfile_dir = NULL,
  filename = NULL,
  button_label = paste0("Download: ", "<code>", filename, "</code>"),
  output_extension = ".rds",
  icon = "fa fa-save",
  button_type = "success",
  self_contained = TRUE,
  add_download_button = TRUE,
  verbose = TRUE
)
```

# Arguments

object R object to serialize.

save\_output Default FALSE. If TRUE, all outputs (tables and plots) of the analysis will be

saved in a folder (EpiCompare\_file).

outfile\_dir Directory to save the file to.

filename Name of the file to save.

button\_label Character (HTML), button label

output\_extension

Extension of the output file. Currently, .csv, .xlsx, and .rds are supported. If

a (named) list is passed to the function, only .xlsx and .rds are supported.

icon Fontawesome tag e.g.: "fa fa-save"

button\_type Character, one of the standard Bootstrap types

self\_contained A boolean to specify whether your HTML output is self-contained. Default to

FALSE.

add\_download\_button

Add download buttons for each plot or dataset.

verbose Print messages.

### Value

Download button as HTML text.

#### Source

```
csv2 Issue.
Plotly Issue
```

#### **Examples**

```
button <- download_button(object=mtcars)</pre>
```

encode\_H3K27ac

Example ChIP-seq peak file

#### **Description**

Human H3K27ac peak file generated with ChIP-seq using K562 cell-line. Human genome build hg19 was used. The peak file (.BED) was obtained from ENCODE project (https://www.encodeproject.org/files/ENCFF044JNJ/). The BED file was then imported as an GRanges object. Peaks located on chromosome 1 were subsetted to reduce the dataset size.

#### Usage

```
data("encode_H3K27ac")
```

#### **Format**

An object of class GRanges of length 5142.

#### Source

The code to prepare the .Rda file from the raw peak file is:

```
# dataset was directly downloaded from
# https://www.encodeproject.org/files/ENCFF044JNJ/encode_H3K27ac <- ChIPseeker::readPeakFile("patas = "GRanges")
encode_H3K27ac <-encode_H3K27ac[seqnames(encode_H3K27ac) == "chr1"]
my_label <- c("name", "score", "strand", "signalValue", "pValue", "qValue", "peak")
colnames(GenomicRanges::mcols(encode_H3K27ac)) <- my_label
usethis::use_data(encode_H3K27ac, overwrite = TRUE)</pre>
```

EpiCompare

Compare epigenomic datasets

# Description

This function compares and analyses multiple epigenomic datasets and outputs an HTML report containing all results of the analysis. The report is mainly divided into three sections: (1) General Metrics on Peakfiles, (2) Peak Overlaps and (3) Functional Annotation of Peaks.

#### Usage

```
EpiCompare(
  peakfiles,
  genome_build,
  genome_build_output = "hg19",
  blacklist = NULL,
  picard_files = NULL,
  reference = NULL,
  upset_plot = FALSE,
  stat_plot = FALSE,
  chromHMM_plot = FALSE,
  chromHMM_annotation = "K562",
  chipseeker_plot = FALSE,
  enrichment_plot = FALSE,
  tss_plot = FALSE,
  tss_distance = c(-3000, 3000),
  precision_recall_plot = FALSE,
  n_{threshold} = 20,
  corr_plot = FALSE,
  bin_size = 5000,
  interact = TRUE,
  add_download_button = FALSE,
  save_output = FALSE,
  output_filename = "EpiCompare",
  output_timestamp = FALSE,
  output_dir,
  display = NULL,
  run_all = FALSE,
  workers = 1,
  quiet = FALSE,
  error = FALSE,
  debug = FALSE
)
```

#### **Arguments**

peakfiles

A list of peak files as GRanges object and/or as paths to BED files. If paths are provided, EpiCompare imports the file as GRanges object. EpiCompare also accepts a list containing a mix of GRanges objects and paths. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If no names are specified, default file names will be assigned.

genome\_build

A named list indicating the human genome build used to generate each of the following inputs:

- "peakfiles": Genome build for the peakfiles input. Assumes genome build is the same for each element in the peakfiles list.
- "reference": Genome build for the reference input.
- "blacklist" : Genome build for the blacklist input.

Example input list:

```
genome_build = list(peakfiles="hg38", reference="hg19", blacklist="hg19")
```

Alternatively, you can supply a single character string instead of a list. This

should *only* be done in situations where all three inputs (peakfiles, reference, blacklist) are of the same genome build. For example: genome\_build = "hg19"

#### genome\_build\_output

Genome build to standardise all inputs to. Liftovers will be performed automatically as needed. Default: "hg19".

blacklist

A GRanges object containing blacklisted genomic regions. Blacklists included in **EpiCompare** are:

- NULL (default): Automatically selects the appropriate blacklist based on the genome\_build\_output argument.
- "hg19\_blacklist": Regions of hg19 genome that have anomalous and/or unstructured signals. hg19\_blacklist
- "hg38\_blacklist": Regions of hg38 genome that have anomalous and/or unstructured signals. hg38\_blacklist
- "mm10\_blacklist": Regions of mm10 genome that have anomalous and/or unstructured signals. mm10\_blacklist
- "mm9\_blacklist": Blacklisted regions of mm10 genome that have been lifted over from mm10\_blacklist. mm9\_blacklist
- <user\_input>: A custom user-provided blacklist in GRanges format.

picard\_files

A list of summary metrics output from Picard. Files must be in data.frame format and listed using list() and named using names(). To import Picard duplication metrics (.txt file) into R as data frame, use:

picard <- read.table("/path/to/picard/output", header = TRUE, fill =
TRUE).</pre>

reference

A named list containing reference peak file(s) as GRanges object. Please ensure that the reference file is listed and named i.e. list("reference\_name" = reference\_peak). If more than one reference is specified, individual reports for each reference will be generated. However, please note that specifying more than one reference can take awhile. If a reference is specified, it enables two analyses: (1) plot showing statistical significance of overlapping/non-overlapping peaks; and (2) ChromHMM of overlapping/non-overlapping peaks.

upset\_plot

Default FALSE. If TRUE, the report includes upset plot of overlapping peaks.

stat\_plot

Default FALSE. If TRUE, the function creates a plot showing the statistical significance of overlapping/non-overlapping peaks. Reference peak file must be provided.

chromHMM\_plot

Default FALSE. If TRUE, the function outputs ChromHMM heatmap of individual peak files. If a reference peak file is provided, ChromHMM annotation of overlapping and non-overlapping peaks is also provided.

#### chromHMM\_annotation

ChromHMM annotation for ChromHMM plots. Default K562 cell-line. Cell-line options are:

- "K562" = K-562 cells
- "Gm12878" = Cellosaurus cell-line GM12878
- "H1hesc" = H1 Human Embryonic Stem Cell
- "Hepg2" = Hep G2 cell
- "Hmec" = Human Mammary Epithelial Cell
- "Hsmm" = Human Skeletal Muscle Myoblasts
- "Huvec" = Human Umbilical Vein Endothelial Cells

- "Nhek" = Normal Human Epidermal Keratinocytes
- "Nhlf" = Normal Human Lung Fibroblasts

chipseeker\_plot

Default FALSE. If TRUE, the report includes a barplot of ChIPseeker annotation of peak files.

enrichment\_plot

Default FALSE. If TRUE, the report includes dotplots of KEGG and GO enrichment analysis of peak files.

Default FALSE. If TRUE, the report includes peak count frequency around transcriptional start site. Note that this can take awhile.

A vector specifying the distance upstream and downstream around transcription start sites (TSS). The default value is c(-3000, 3000); meaning peak frequency 3000bp upstream and downstream of TSS will be displayed.

precision\_recall\_plot

Default is FALSE. If TRUE, creates a precision-recall curve plot and an F1 plot using plot\_precision\_recall.

n\_threshold Number of thresholds to test.

corr\_plot Default is FALSE. If TRUE, creates a correlation plot across all peak files using

plot\_corr.

bin\_size Default of 100. Base-pair size of the bins created to measure correlation. Use smaller value for higher resolution but longer run time and larger memory usage.

interact Default TRUE. By default, plots are interactive. If set FALSE, all plots in the report will be static.

add\_download\_button

Add download buttons for each plot or dataset.

Default FALSE. If TRUE, all outputs (tables and plots) of the analysis will be saved in a folder (EpiCompare\_file).

output\_filename

Default EpiCompare.html. If otherwise, the html report will be saved in the specified name.

output\_timestamp

Default FALSE. If TRUE, date will be included in the file name.

 ${\tt output\_dir} \qquad \quad {\tt Path \ to \ where \ output \ HTML \ file \ should \ be \ saved}.$ 

display After completion, automatically display the HTML report file in one of the following ways:

- "browser" : Display the report in your default web browser.
- "rsstudio" : Display the report in Rstudio.
- NULL (default): Do not display the report.

run\_all Convenience argument that enables all plots/features (without specifying each argument manually) by overriding the default values. Default: FALSE.

workers Number of threads to parallelize across.

quiet An option to suppress printing during rendering from knitr, pandoc command line and others. To only suppress printing of the last "Output created: " message,

you can set rmarkdown.render.message to FALSE

error If TRUE, the Rmarkdown report will continue to render even when some chunks

encounter errors (default: FALSE). Passed to opts\_chunk.

debug Run in debug mode, where are messages and warnings are printed within the

HTML report (default: FALSE).

20 fig\_length

#### Value

Path to one or more HTML report files.

#### **Examples**

```
### Load Data ###
data("encode_H3K27ac") # example dataset as GRanges object
data("CnT_H3K27ac") # example dataset as GRanges object
data("CnR_H3K27ac") # example dataset as GRanges object
data("CnT_H3K27ac_picard") # example Picard summary output
data("CnR_H3K27ac_picard") # example Picard summary output
#### Prepare Input ####
# create named list of peakfiles
peakfiles <- list(CnR=CnR_H3K27ac, CnT=CnT_H3K27ac)</pre>
# create named list of picard outputs
picard_files <- list(CnR=CnR_H3K27ac_picard, CnT=CnT_H3K27ac_picard)</pre>
# reference peak file
reference <- list("ENCODE" = encode_H3K27ac)</pre>
### Run EpiCompare ###
output_html <- EpiCompare(peakfiles = peakfiles,</pre>
           genome_build = list(peakfiles="hg19",
                                reference="hg19"),
           picard_files = picard_files,
           reference = reference,
           output_filename = "EpiCompare_test",
           output_dir = tempdir())
# utils::browseURL(output_html)
```

fig\_length

Dynamic Figure Length Generator

#### **Description**

This function calculates the appropriate figure height depending on the number of items.

#### Usage

```
fig_length(default_size, number_of_items, max_items)
```

#### **Arguments**

```
default_size The default figure length. Must be numeric.
number_of_items
Number of peak files, or terms.
max_items Maximum number of peak files, or terms.
```

#### Value

Figure height/width. A number.

fragment\_info 21

fragment\_info

Summary on fragments

# Description

This function outputs a summary on fragments using metrics generated by Picard. Provides the number of mapped fragments, duplication rate and number of unique fragments.

### Usage

```
fragment_info(picard_list)
```

# **Arguments**

picard\_list

Named list of duplication metrics generated by Picard as data frame. Data frames must be named and listed using list(). e.g. list("name1"=file1, "name2"=file2). To import Picard duplication metrics (.txt file) into R as data frame, use picard <- read.table("/path/to/picard/output", header = TRUE, fill = TRUE).

#### Value

A table summarizing metrics on fragments.

### **Examples**

gather\_files

Gather files

# Description

Recursively find peak/picard files stored within subdirectories and import them as a list of GRanges objects.

22 gather\_files

#### Usage

```
gather_files(
   dir,
   type = "peaks.stringent",
   nfcore_cutandrun = FALSE,
   return_paths = FALSE,
   rbind_list = FALSE,
   workers = check_workers(),
   verbose = TRUE
)
```

### **Arguments**

dir Directory to search within.

type File type to search for. Options include:

- "<pattern>"Finds files matching an arbitrary regex pattern specified by user.
- "peaks.stringent"Finds files ending in "\*.stringent.bed\$"
- "peaks.consensus"Finds files ending in "\*.consensus.peaks.bed\$"
- "peaks.consensus.filtered" Finds files ending in"\*.consensus.peaks.filtered.awk.bed\$"
- "picard"Finds files ending in "\*.target.markdup.MarkDuplicates.metrics.txt\$"

nfcore\_cutandrun

Whether the files were generated by the nf-core/cutandrun Nextflow pipeline. If TRUE, can use the standardised folder structure to automatically generate more

descriptive file names with sample IDs.

return\_paths Return only the file paths without actually reading them in as GRanges.

rbind\_list Bind all objects into one.

workers Number of cores to parallelise across (in applicable functions). If NULL, will set

to the total number of available cores minus 1.

verbose Print messages.

#### **Details**

For "peaks.stringent" files called with SEACR, column names will be automatically added:

- total\_signal: Total signal contained within denoted coordinates.
- max\_signalMaximum bedgraph signal attained at any base pair within denoted coordinates.
- max\_signal\_region Region representing the farthest upstream and farthest downstream bases within the denoted coordinates that are represented by the maximum bedgraph signal.

# Value

A named list of GRanges objects.

#### **Examples**

gather\_files\_names 23

gather\_files\_names

Make file names

#### **Description**

Support function for gather\_files.

#### Usage

```
gather_files_names(paths, type, nfcore_cutandrun, verbose = TRUE)
```

### **Arguments**

paths

Character vector of file paths.

type

File type to search for. Options include:

- "<pattern>"Finds files matching an arbitrary regex pattern specified by user.
- "peaks.stringent"Finds files ending in "\*.stringent.bed\$"
- "peaks.consensus"Finds files ending in "\*.consensus.peaks.bed\$"
- "peaks.consensus.filtered" Finds files ending in"\*.consensus.peaks.filtered.awk.bed\$"
- "picard"Finds files ending in "\*.target.markdup.MarkDuplicates.metrics.txt\$"

nfcore\_cutandrun

Whether the files were generated by the nf-core/cutandrun Nextflow pipeline. If TRUE, can use the standardised folder structure to automatically generate more descriptive file names with sample IDs.

Print messages.

verbose

### Value

Named character vector.

get\_bpparam

Get BiocParallel parameters

### **Description**

Get (and optionally register) BiocParallel parameter (BPPARAM). SnowParam is the default function as it tends to be more robust. However, because it doesn't work on Windows, this function automatically detected the Operating System and switches to SerialParam as needed.

```
get_bpparam(
  workers,
  progressbar = workers > 1,
  use_snowparam = TRUE,
  register_now = FALSE
)
```

#### **Arguments**

workers Number of threads to parallelize across.

progressbar logical(1) Enable progress bar (based on plyr:::progress\_text).

use\_snowparam Whether to use SnowParam (default: TRUE) or MulticoreParam (FALSE) when

parallelising across multiple workers.

register\_now Register the cores now with register (TRUE), or simply return the BPPARAM object

(default: FALSE).

#### Value

**BPPARAM** 

```
get_chromHMM_annotation
```

Download ChromHMM annotation file(s)

# Description

Download ChromHMM annotation file(s) for a given cell-line (returned as a GRanges object) or a list of cell-lines (returned as a named list of GRanges objects). All annotations are aligned to the hg19 genome build. All data can be found on the UCSC Genome Browser here.

### Usage

```
get_chromHMM_annotation(
  cell_line,
  cache = BiocFileCache::BiocFileCache(ask = FALSE)
)
```

# **Arguments**

cell\_line

ChromHMM annotation for user-specified cell-line. Cell-line options are:

- "K562" = K-562 cells
- "Gm12878" = Cellosaurus cell-line GM12878
- "H1hesc" = H1 Human Embryonic Stem Cell
- "Hepg2" = Hep G2 cell
- "Hmec" = Human Mammary Epithelial Cell
- "Hsmm" = Human Skeletal Muscle Myoblasts
- "Huvec" = Human Umbilical Vein Endothelial Cells
- "Nhek" = Normal Human Epidermal Keratinocytes
- "Nhlf" = Normal Human Lung Fibroblasts

### Value

Cell-line specific ChromHMM annotation file. Default K562 cell-line.

group\_files 25

group_files	Group files
61 0ap_11103	Group jues

#### **Description**

Assign group names to each file in a named list based on a series of string searches based on combinations of relevant metadata factors.

#### Usage

```
group_files(peakfiles, searches)
```

### **Arguments**

peakfiles A list of peak files as GRanges object and/or as paths to BED files. If paths

are provided, EpiCompare imports the file as GRanges object. EpiCompare also accepts a list containing a mix of GRanges objects and paths. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If no

names are specified, default file names will be assigned.

searches A named list of substrings to group peakfiles by.

#### Value

Named peak files

# Examples

hg19\_blacklist

Human genome hg19 blacklisted regions

# Description

Obtained from <a href="https://www.encodeproject.org/files/ENCFF001TD0">https://www.encodeproject.org/files/ENCFF001TD0</a>. The ENCODE blacklist includes regions of the hg19 genome that have anomalous and/or unstructured signals independent of the cell-line or experiment. Removal of ENCODE blacklist is recommended for quality measure.

```
data("hg19_blacklist")
```

26 hg38\_blacklist

#### **Format**

An object of class GRanges of length 411.

#### Source

The code to prepare the .Rda file is:

```
# blacklisted regions were directly downloaded
# from https://www.encodeproject.org/files/ENCFF001TDO/
hg19_blacklist <-ChIPseeker::readPeakFile(file.path(path), as = "GRanges")
usethis::use_data(hg19_blacklist, overwrite = TRUE)</pre>
```

hg38\_blacklist

Human genome hg38 blacklisted regions

# Description

Obtained from https://www.encodeproject.org/files/ENCFF356LFX/. The ENCODE black-list includes regions of the hg38 genome that have anomalous and/or unstructured signals independent of the cell-line or experiment. Removal of ENCODE blacklist is recommended for quality measure.

### Usage

```
data("hg38_blacklist")
```

### **Format**

An object of class GRanges of length 910.

#### Source

The code to prepare the .Rda file is:

```
## blacklisted regions were directly downloaded
## from https://www.encodeproject.org/files/ENCFF356LFX/
hg38_blacklist <-ChIPseeker::readPeakFile(file.path(path), as = "GRanges")
usethis::use_data(hg38_blacklist, overwrite = TRUE)</pre>
```

is\_granges 27

is\_granges

Is an object of class GRanges

#### **Description**

Check whether an object is of the class GRanges.

#### Usage

```
is_granges(obj)
```

# Arguments

obj

Any R object.

### Value

Boolean.

liftover\_grlist

Liftover peak list

### **Description**

Perform genome build liftover to one or more GRanges objects at once.

# Usage

```
liftover_grlist(
  grlist,
  input_build,
  output_build = "hg19",
  style = "UCSC",
  keep_chr = paste0("chr", c(seq_len(22), "X", "Y")),
  as_grangeslist = FALSE,
  merge_all = FALSE,
  verbose = TRUE
)
```

# Arguments

grlist A named list of GRanges objects, or simply a single unlisted GRanges object.

Can perform liftover within species or across species.

input\_build The genome build of grlist.

output\_build Desired genome build for grlist to be lifted over to.

style Chromosome style, set by seqlevelsStyle.

• "UCSC": Uses the chromosome style "chr1".

• "NCBI": Uses the chromosome style "1"

28 messager

```
keep_chr Which chromosomes to keep.

as_grangeslist Return as a GRangesList.

merge_all Merge all GRanges into a single GRanges object.

verbose Print messages.
```

#### Value

Named list of lifted GRanges objects.

### **Examples**

messager

Print messages

# **Description**

Conditionally print messages. Allows developers to easily control verbosity of functions, and meet Bioconductor requirements that dictate the message must first be stored to a variable before passing to message.

# Usage

```
messager(..., v = TRUE, parallel = FALSE)
```

# **Arguments**

v Whether to print messages or not.

parallel Whether to enable message print when wrapped in parallelised functions.

#### Value

Null

message\_parallel 29

message\_parallel

Message parallel

# Description

Send messages to console even from within parallel processes

#### Usage

```
message_parallel(...)
```

#### Value

A message

mm10\_blacklist

Mouse genome mm10 blacklisted regions

### **Description**

Obtained from <a href="https://www.encodeproject.org/files/ENCFF547MET/">https://www.encodeproject.org/files/ENCFF547MET/</a>. The ENCODE blacklist includes regions of the mm10 genome that have anomalous and/or unstructured signals independent of the cell-line or experiment. Removal of ENCODE blacklist is recommended for quality measure.

# Usage

```
data("mm10_blacklist")
```

### **Format**

An object of class GRanges of length 164.

### Source

The code to prepare the .Rda file is:

```
## blacklisted regions were directly downloaded
## from https://www.encodeproject.org/files/ENCFF547MET/
mm10_blacklist <-ChIPseeker::readPeakFile(file.path(path), as = "GRanges")
usethis::use_data(mm10_blacklist, overwrite = TRUE)</pre>
```

30 overlap\_heatmap

mm9_blacklist	Mouse genome mm9 blacklisted regions	

### **Description**

Blaklisted regions of the mm9 genome build brained by lifting over the mm10\_blacklist.

### Usage

```
data("mm9_blacklist")
```

#### **Format**

An object of class GRanges of length 292.

### Source

```
tmp <- base::get("mm10_blacklist", asNamespace("EpiCompare")) mm9_blacklist <- liftover_grlist(grl
= tmp, input_build = "mm10", output_build = "mm9", keep_chr = NULL) usethis::use_data(mm9_blacklist,
overwrite = TRUE)
```

overlap\_heatmap

Generate heatmap of percentage overlap

# Description

This function generates a heatmap showing percentage of overlapping peaks between peak files.

### Usage

```
overlap_heatmap(
  peaklist,
  interact = TRUE,
  draw_cellnote = TRUE,
  fill_diag = NA,
  verbose = TRUE
)
```

# Arguments

peaklist	A list of peak files as GRanges object. Files must be listed and named using list(). e.g. list("name1"=file1, "name2"=file2). If not named, default file names will be assigned.
interact	Default TRUE. By default heatmap is interactive. If FALSE, heatmap is static.
draw_cellnote	Draw the numeric values within each heatmap cell.
fill_diag	Fill the diagonal of the overlap matrix.
verbose	Print messages.

overlap\_percent 31

#### Value

An interactive heatmap

### **Examples**

```
### Load Data ###
data("encode_H3K27ac") # example peakfile GRanges object
data("CnT_H3K27ac") # example peakfile GRanges object
### Create Named List ###
peaklist <- list("encode"=encode_H3K27ac, "CnT"=CnT_H3K27ac)
### Run ###
my_heatmap <- overlap_heatmap(peaklist = peaklist)</pre>
```

overlap\_percent

Calculate percentage of overlapping peaks

### Description

This function calculates the percentage of overlapping peaks and outputs a table or matrix of results.

### Usage

```
overlap_percent(
  peaklist1,
  peaklist2,
  invert = FALSE,
  precision_recall = TRUE,
  suppress_messages = TRUE
)
```

#### **Arguments**

peaklist1 A list of peak files as GRanges object. Files must be listed and named using list(). e.g. list("name1"=file1, "name2"=file2). If not named, default

file names will be assigned.

peaklist2 peaklist1 A list of peak files as GRanges object. Files must be listed and named

using list(). e.g. list("name1"=file1, "name2"=file2).

invert If TRUE, keep only the ranges in x that do *not* overlap ranges.

precision\_recall

Return percision-recall results for all combinations of peaklist1 (the "query") and peaklist2 (the "subject"). See <a href="mailto:subject">subsetByOverlaps</a> for more details on this

terminology.

suppress\_messages

Suppress messages.

### Value

data frame

32 overlap\_stat\_plot

#### **Examples**

overlap\_stat\_plot

Statistical significance of overlapping peaks

#### **Description**

This function calculates the statistical significance of overlapping/ non-overlapping peaks against a reference peak file. If the reference peak file has the BED6+4 format (peak called by MACS2), the function generates a series of box plots showing the distribution of q-values for sample peaks that are overlapping and non-overlapping with the reference. If the reference peak file does not have the BED6+4 format, the function uses enrichPeakOverlap from **ChIPseeker** package to calculate the statistical significance of overlapping peaks only. In this case, please provide an annotation file as a TxDb object.

### Usage

```
overlap_stat_plot(
  reference,
  peaklist,
  txdb = NULL,
  interact = FALSE,
  nShuffle = 50,
  digits = 4,
  workers = check_workers()
)
```

### Arguments

reference	A reference peak file as GRanges object.
peaklist	A list of peak files as GRanges object. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If not named, default file names will be assigned.
txdb	A TxDb annotation object from Bioconductor. This is required only if the reference file does not have BED6+4 format.
interact	Default TRUE. By default, plots are interactive. If set FALSE, all plots in the report will be static.
nShuffle	shuffle numbers

overlap\_upset\_plot 33

digits integer indicating the number of decimal places (round) or significant digits

(signif) to be used. For round, negative values are allowed (see 'Details').

workers Number of threads to parallelize across.

#### Value

A named list.

• "plot"boxplot/barplot showing the statistical significance of overlapping/non-overlapping peaks.

• "data"Plot data.

#### **Examples**

overlap\_upset\_plot

Generate Upset plot for overlapping peaks

### **Description**

This function generates upset plot of overlapping peaks files using the **ComplexUpset** package.

#### Usage

```
overlap_upset_plot(peaklist, verbose = TRUE)
```

#### **Arguments**

peaklist A named list of peak files as GRanges object. Objects must be listed and named

using list(). e.g. list("name1"=file1, "name2"=file2). If not named,

default file names are assigned.

verbose Print messages

#### Value

Upset plot of overlapping peaks.

### **Examples**

```
### Load Data ###
data("encode_H3K27ac") # load example data
data("CnT_H3K27ac") # load example data
peaklist <- list("encode"=encode_H3K27ac, "CnT"=CnT_H3K27ac)
my_plot <- overlap_upset_plot(peaklist = peaklist)</pre>
```

peak\_info

Summary of Peak Information

#### **Description**

This function outputs a table summarizing information on the peak files. Provides the total number of peaks and the percentage of peaks in blacklisted regions.

#### Usage

```
peak_info(peaklist, blacklist)
```

#### **Arguments**

peaklist A named list of peak files as GRanges object. Objects listed using list("name1"

= peak, "name2" = peak2).

blacklist A GRanges object containing blacklisted regions.

#### Value

A summary table of peak information

### **Examples**

plot\_ChIPseeker\_annotation

Create ChIPseeker annotation plot

### **Description**

This function annotates peaks using ChIPseeker::annotatePeak. It outputs functional annotation of each peak file in a barplot.

```
plot_ChIPseeker_annotation(
  peaklist,
  txdb = NULL,
  tss_distance = c(-3000, 3000),
  interact = FALSE
)
```

plot\_chromHMM 35

#### **Arguments**

peaklist A list of peak files as GRanges object. Files must be listed and named using

list(). e.g. list("name1"=file1, "name2"=file2). If not named, default

file names will be assigned.

txdb A TxDb annotation object from Bioconductor.

tss\_distance A vector specifying the distance upstream and downstream around transcription

start sites (TSS). The default value is c(-3000, 3000); meaning peak frequency

3000bp upstream and downstream of TSS will be displayed.

interact Default TRUE. By default, plots are interactive. If set FALSE, all plots in the

report will be static.

#### Value

ggplot barplot

#### **Examples**

plot\_chromHMM

Plot ChromHMM heatmap

#### **Description**

Creates a heatmap using outputs from ChromHMM using ggplot2. The function takes a list of peakfiles, performs ChromHMM and outputs a heatmap. ChromHMM annotation file must be loaded prior to using this function. ChromHMM annotations are aligned to hg19, and will be automatically lifted over to the genome\_build to match the build of the peaklist.

```
plot_chromHMM(
   peaklist,
   chromHMM_annotation,
   genome_build,
   cell_line = NULL,
   interact = FALSE,
   return_data = FALSE
)
```

36 plot\_corr

#### **Arguments**

peaklist A named list of peak files as GRanges object. If list is not named, default names will be assigned.

chromHMM\_annotation

ChromHMM annotation list.

genome\_build The human genome reference build used to generate peakfiles. "hg19" or "hg38".

cell\_line If not cell\_line, will replace chromHMM\_annotation by importing chromHMM data for a given cell line using get\_chromHMM\_annotation.

interact Default TRUE. By default, the heatmaps are interactive. IfFALSE, the function generates a static ChromHMM heatmap.

Return the plot data as in addition to the plot itself.

#### Value

return\_data

ChromHMM heatmap, or a named list.

### **Examples**

plot\_corr

Plot correlation of peak files

# Description

Plot correlation by binning genome and measuring correlation of peak quantile ranking. This ranking is based on p-value or other peak intensity measure dependent on the peak calling approach.

```
plot_corr(
  peakfiles,
  reference = NULL,
  genome_build,
  bin_size = 5000,
  keep_chr = NULL,
  drop_empty_chr = FALSE,
  method = "spearman",
  intensity_cols = c("total_signal", "qValue", "Peak Score", "score"),
  interact = FALSE,
  draw_cellnote = TRUE,
  fill_diag = NA,
```

plot\_corr 37

```
workers = check_workers(),
 show_plot = TRUE
 save_path = tempfile(fileext = ".corr.csv.gz")
)
```

## Arguments

peakfiles

A list of peak files as GRanges object and/or as paths to BED files. If paths are provided, EpiCompare imports the file as GRanges object. EpiCompare also accepts a list containing a mix of GRanges objects and paths. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If no names are specified, default file names will be assigned.

reference

A named list containing reference peak file(s) as GRanges object. Please ensure that the reference file is listed and named i.e. list("reference\_name" = reference\_peak). If more than one reference is specified, individual reports for each reference will be generated. However, please note that specifying more than one reference can take awhile. If a reference is specified, it enables two analyses: (1) plot showing statistical significance of overlapping/nonoverlapping peaks; and (2) ChromHMM of overlapping/non-overlapping peaks.

genome\_build

The build of \*\*all\*\* peak and reference files to calculate the correlation matrix on. If all peak and reference files are not of the same build use liftover\_grlist to convert them all before running. Genome build should be one of hg19, hg38, mm9, mm10.

bin\_size

Default of 100. Base-pair size of the bins created to measure correlation. Use smaller value for higher resolution but longer run time and larger memory usage.

keep\_chr

Which chromosomes to keep.

drop\_empty\_chr Drop chromosomes that are not present in any of the peakfiles (default: FALSE).

method

Default spearman (i.e. non-parametric). A character string indicating which correlation coefficient (or covariance) is to be computed. One of "pearson", "kendall", or "spearman": can be abbreviated.

intensity\_cols Depending on which columns are present, this value will be used to get quantiles and ultimately calculate the correlations:

- "total\_signal" : Used by the peak calling software SEACR. NOTE: Another SEACR column (e.g. "max\_signal") can be used together or instead of "total\_signal".
- "qValue"Used by the peak calling software MACS2/3. Should contain the negative log of the p-values after multiple testing correction.
- "Peak Score": Used by the peak calling software **HOMER**.

Default TRUE. By default heatmap is interactive. If FALSE, heatmap is static. interact

draw\_cellnote Draw the numeric values within each heatmap cell.

fill\_diag Fill the diagonal of the overlap matrix. workers Number of threads to parallelize across.

Show the plot. show\_plot

Path to save a table of correlation results to. save\_path

## Value

list with correlation plot (corr\_plot) and correlation matrix (data)

38 plot\_enrichment

#### **Examples**

plot\_enrichment

Generate enrichment analysis plots

## **Description**

This function runs KEGG and GO enrichment analysis of peak files and generates dot plots.

## Usage

```
plot_enrichment(
  peaklist,
  txdb = NULL,
  tss_distance = c(-3000, 3000),
  pvalueCutoff = 0.05,
  interact = FALSE,
  verbose = TRUE
)
```

## **Arguments**

peaklist A list of peak files as GRanges object. Files must be listed and named using

list(). e.g. list("name1"=file1, "name2"=file2). If not named, default

file names will be assigned.

txdb A TxDb annotation object from Bioconductor.

tss\_distance A vector specifying the distance upstream and downstream around transcription

start sites (TSS). The default value is c(-3000, 3000); meaning peak frequency

3000bp upstream and downstream of TSS will be displayed.

pvalueCutoff P-value cutoff, passed to compareCluster.

interact Default TRUE. By default, plots are interactive. If set FALSE, all plots in the

report will be static.

verbose Print messages.

## Value

KEGG and GO dot plots

plot\_precision\_recall 39

#### **Examples**

plot\_precision\_recall Plot precision-recall curves

## Description

Plot precision-recall curves (and optionally F1 plots) by iteratively testing for peak overlap across a series of thresholds used to filter peakfiles. Each GRanges object in peakfiles will be used as the "query" against each GRanges object in reference as the subject. Will automatically use any columns that are specified with thresholding\_cols and present within each GRanges object to create percentiles for thresholding. *NOTE*: Assumes that all GRanges in peakfiles and reference are already aligned to the same genome build.

## Usage

```
plot_precision_recall(
  peakfiles,
  reference,
  thresholding_cols = c("total_signal", "qValue", "Peak Score"),
  initial_threshold = 0,
  n_{threshold} = 20,
  max_threshold = 1,
  workers = check_workers(),
  plot_f1 = TRUE,
  subtitle = NULL,
  color = "peaklist1",
  shape = color,
  facets = "peaklist2 ~ .",
  interact = FALSE,
  show_plot = TRUE,
  save_path = tempfile(fileext = "precision_recall.csv"),
  verbose = TRUE
)
```

#### **Arguments**

peakfiles

A list of peak files as GRanges object and/or as paths to BED files. If paths are provided, EpiCompare imports the file as GRanges object. EpiCompare also accepts a list containing a mix of GRanges objects and paths. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If no names are specified, default file names will be assigned.

40 plot\_precision\_recall

reference

A named list containing reference peak file(s) as GRanges object. Please ensure that the reference file is listed and named i.e. list("reference\_name" = reference\_peak). If more than one reference is specified, individual reports for each reference will be generated. However, please note that specifying more than one reference can take awhile. If a reference is specified, it enables two analyses: (1) plot showing statistical significance of overlapping/non-overlapping peaks; and (2) ChromHMM of overlapping/non-overlapping peaks.

#### thresholding\_cols

Depending on which columns are present, GRanges will be filtered at each threshold according to one or more of the following:

- "total\_signal": Used by the peak calling software SEACR. NOTE: Another SEACR column (e.g. "max\_signal") can be used together or instead of "total\_signal".
- "qValue"Used by the peak calling software MACS2/3. Should contain the negative log of the p-values after multiple testing correction.
- "Peak Score": Used by the peak calling software HOMER.

initial\_threshold

Numeric threshold that was provided to SEACR (via the parameter --ctrl) when calling peaks without an IgG control.

n\_threshold Number of thresholds to test.max\_threshold Maximum threshold to test.

workers Number of threads to parallelize across.

plot\_f1 Generate a plot with the F1 score vs. threshold as well.

subtitle Plot subtitle.

color Variable to color data points by.
shape Variable to set data point shapes by.

facets [Deprecated] Please use rows and cols instead.

interact Default TRUE. By default, plots are interactive. If set FALSE, all plots in the

report will be static.

show\_plot Show the plot.

save\_path File path to save precision-recall results to.

verbose Print messages.

#### Value

list with data and precision recall and F1 plots

precision\_recall 41

precision\_recall

Compute precision-recall

#### **Description**

Compute precision and recall using each GRanges object in peakfiles as the "query" against each GRanges object in reference as the subject.

#### Usage

```
precision_recall(
  peakfiles,
  reference,
  thresholding_cols = c("total_signal", "qValue", "Peak Score"),
  initial_threshold = 0,
  n_threshold = 20,
  max_threshold = 1,
  cast = TRUE,
  workers = 1,
  verbose = TRUE,
  save_path = tempfile(fileext = "precision_recall.csv"),
  ...
)
```

#### **Arguments**

peakfiles

A list of peak files as GRanges object and/or as paths to BED files. If paths are provided, EpiCompare imports the file as GRanges object. EpiCompare also accepts a list containing a mix of GRanges objects and paths. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If no names are specified, default file names will be assigned.

reference

A named list containing reference peak file(s) as GRanges object. Please ensure that the reference file is listed and named i.e. list("reference\_name" = reference\_peak). If more than one reference is specified, individual reports for each reference will be generated. However, please note that specifying more than one reference can take awhile. If a reference is specified, it enables two analyses: (1) plot showing statistical significance of overlapping/non-overlapping peaks; and (2) ChromHMM of overlapping/non-overlapping peaks.

thresholding\_cols

Depending on which columns are present, GRanges will be filtered at each threshold according to one or more of the following:

- "total\_signal": Used by the peak calling software SEACR. NOTE: Another SEACR column (e.g. "max\_signal") can be used together or instead of "total\_signal".
- "qValue"Used by the peak calling software MACS2/3. Should contain the negative log of the p-values after multiple testing correction.
- "Peak Score": Used by the peak calling software **HOMER**.

initial\_threshold

Numeric threshold that was provided to SEACR (via the parameter --ctrl) when calling peaks without an IgG control.

n\_threshold Number of thresholds to test.max\_threshold Maximum threshold to test.

cast Cast the data into a format that's more compatible with **ggplot2**.

workers Number of threads to parallelize across.

verbose Print messages.

save\_path File path to save precision-recall results to.

Arguments passed on to bpplapply

apply\_fun Iterator function to use.

 ${\tt register\_now}\ \ Register\ the\ cores\ now\ with\ {\tt register}\ ({\tt TRUE}), or\ simply\ return\ the$ 

BPPARAM object (default: FALSE).

 $use\_snowparam\ Whether\ to\ use\ SnowParam\ (default:\ TRUE)\ or\ MulticoreParam$ 

(FALSE) when parallelising across multiple workers.

progressbar logical(1) Enable progress bar (based on plyr:::progress\_text).

X Any object for which methods length, [, and [[ are implemented.

FUN The function to be applied to each element of X.

#### Value

Overlap

## **Examples**

```
{\tt precision\_recall\_matrix}
```

Create a precision-recall matrix

#### Description

Converts a list of peak files to a symmetric matrix where the y-axis indicates precision and the x-axis indicates recall.

# Usage

```
precision_recall_matrix(peaklist, fill_diag = NA, verbose = TRUE)
```

## **Arguments**

fill\_diag Fill the diagonal of the overlap matrix.

verbose Print messages.

#### Value

matrix

```
predict_precision_recall
```

Predict precision-recall

## Description

Predict specific values of precision or recall by fitting a model to a precision-recall curve. Predictions that are <0 will automatically be set to 0. Predictions that are >100 will automatically be set to 100.

## Usage

```
predict_precision_recall(
  pr_df,
  fun = stats::loess,
  precision = seq(10, 100, 10),
  recall = seq(10, 100, 10)
)
```

## **Arguments**

pr\_df Precision-recall data.frame generated by precision\_recall.

fun Function to fit the data with.

precision Precision values to predict recall from.

recall Recall values to predict precision from.

#### Value

A named list of fitted models and predictions.

## Source

Fix for producing NAs from loess fun.

44 prepare\_blacklist

predict\_values

Predict values

## **Description**

Fit a model and make predictions from it.

## Usage

```
predict_values(df, fun, values, input_var, predicted_var)
```

## **Arguments**

df data.frame

fun Function to fit the data with.

values Values to make predictions from.

input\_var Input variable column name.

predicted\_var Predicted variable name.

#### Value

data.frame

prepare\_blacklist

Prepare blacklist as GRanges

## Description

Selects the appropriate blacklist in a variety of conditions.

## Usage

```
prepare_blacklist(
  blacklist,
  output_build,
  blacklist_build = NULL,
  verbose = TRUE
)
```

## **Arguments**

 ${\tt output\_build} \qquad {\tt Desired \ genome \ build \ for \ grlist \ to \ be \ lifted \ over \ to}.$ 

blacklist\_build

Genome build of the blacklist. Only used when blacklist is a user-supplied

GRanges object.

verbose Print messages.

#### Value

A GRanges objects of blacklisted genomic regions from the relevant genome build.

prepare\_genome\_builds Prepare genome builds

## **Description**

Parse the genome\_build argument into peaklist\_build and reference\_build.

## Usage

```
prepare_genome_builds(genome_build, blacklist = NULL)
```

#### **Arguments**

genome\_build

A named list indicating the human genome build used to generate each of the following inputs:

- "peakfiles": Genome build for the peakfiles input. Assumes genome build is the same for each element in the peakfiles list.
- "reference": Genome build for the reference input.
- "blacklist": Genome build for the blacklist input.

#### Example input list:

```
genome_build = list(peakfiles="hg38", reference="hg19", blacklist="hg19")
```

Alternatively, you can supply a single character string instead of a list. This should *only* be done in situations where all three inputs (peakfiles, reference, blacklist) are of the same genome build. For example: genome\_build = "hg19"

blacklist

A GRanges object containing blacklisted genomic regions. Blacklists included in **EpiCompare** are:

- NULL (default): Automatically selects the appropriate blacklist based on the genome\_build\_output argument.
- "hg19\_blacklist": Regions of hg19 genome that have anomalous and/or unstructured signals. hg19\_blacklist
- "hg38\_blacklist": Regions of hg38 genome that have anomalous and/or unstructured signals. hg38\_blacklist
- "mm10\_blacklist": Regions of mm10 genome that have anomalous and/or unstructured signals. mm10\_blacklist
- "mm9\_blacklist": Blacklisted regions of mm10 genome that have been lifted over from mm10\_blacklist. mm9\_blacklist
- <user\_input>: A custom user-provided blacklist in GRanges format.

#### Value

Named list.

46 prepare\_reference

## **Description**

Prepare peaklist as GRanges

## Usage

```
prepare_peaklist(peaklist, remove_empty = TRUE, as_grangeslist = FALSE)
```

## **Arguments**

peaklist A named list of peaks as GRanges or paths to BED files.
remove\_empty Remove any empty elements in the list.
as\_grangeslist Convert output to class GRangesList before returning.

#### Value

A list of GRanges objects

prepare\_reference

Prepare reference as GRanges

## **Description**

Prepare reference as GRanges

## Usage

```
prepare_reference(
  reference,
  max_elements = NULL,
  remove_empty = TRUE,
  as_list = TRUE,
  as_grangeslist = FALSE
)
```

## **Arguments**

reference A named list of GRanges objects, or a single GRanges object to be converted

into a named list.

max\_elements Max number of elements to use within the list. Set to NULL (default) to use all

elements.

remove\_empty Remove any empty elements in the list.

as\_list Return as a list.

as\_grangeslist Return as a GRangesList (overrides as\_list).

## Value

A list of GRanges objects

read\_bowtie 47

read\_bowtie

Read bowtie

## **Description**

Read a bowtie file.

# Usage

```
read_bowtie(path, verbose = TRUE)
```

## Arguments

path Path to bowtie file. verbose Print messages.

## Value

data.table

read\_peaks

Read peaks

# Description

Read peak files.

## Usage

```
read_peaks(path, type, verbose = TRUE)
```

## **Arguments**

path

Path to peak file.

type

File type to search for. Options include:

- "<pattern>"Finds files matching an arbitrary regex pattern specified by user.
- "peaks.stringent"Finds files ending in "\*.stringent.bed\$"
- "peaks.consensus"Finds files ending in "\*.consensus.peaks.bed\$"
- "peaks.consensus.filtered" Finds files ending in"\*.consensus.peaks.filtered.awk.bed\$"
- "picard"Finds files ending in "\*.target.markdup.MarkDuplicates.metrics.txt\$"

verbose

Print messages.

#### Value

GRanges

48 rebin\_peaks

Rebin peaks rebin\_peaks

#### **Description**

Standardise a list of peak files by rebinning them into fixd-width tiles across the genome.

#### Usage

```
rebin_peaks(
  peakfiles,
  genome_build,
  intensity_cols = c("total_signal", "qValue", "Peak Score", "score"),
  bin_size = 5000,
  keep\_chr = NULL,
  sep = c(":", "-"),
  drop_empty_chr = FALSE,
  as\_sparse = TRUE,
 workers = check_workers(),
  verbose = TRUE,
)
```

## **Arguments**

peakfiles

A list of peak files as GRanges object and/or as paths to BED files. If paths are provided, EpiCompare imports the file as GRanges object. EpiCompare also accepts a list containing a mix of GRanges objects and paths. Files must be listed and named using list(). E.g. list("name1"=file1, "name2"=file2). If no names are specified, default file names will be assigned.

genome\_build

The build of \*\*all\*\* peak and reference files to calculate the correlation matrix on. If all peak and reference files are not of the same build use liftover\_grlist to convert them all before running. Genome build should be one of hg19, hg38, mm9, mm10.

intensity\_cols Depending on which columns are present, this value will be used to get quantiles and ultimately calculate the correlations:

- "total\_signal" : Used by the peak calling software **SEACR**. *NOTE*: Another SEACR column (e.g. "max\_signal") can be used together or instead of "total signal".
- "qValue"Used by the peak calling software MACS2/3. Should contain the negative log of the p-values after multiple testing correction.
- "Peak Score": Used by the peak calling software HOMER.

bin\_size

Default of 100. Base-pair size of the bins created to measure correlation. Use smaller value for higher resolution but longer run time and larger memory usage.

keep\_chr

Which chromosomes to keep.

sep

Separator to be used after chromosome name (first item) and between start/end genomic coordinates (second item).

drop\_empty\_chr Drop chromosomes that are not present in any of the peakfiles (default: FALSE).

as\_sparse Return the rebinned peaks as a sparse matrix (default: TRUE), which is more efficiently stored than a dense matrix (FALSE). Number of threads to parallelize across. workers verbose Print messages. Arguments passed on to bpplapply apply\_fun Iterator function to use. register\_now Register the cores now with register (TRUE), or simply return the BPPARAM object (default: FALSE). use\_snowparam Whether to use SnowParam (default: TRUE) or MulticoreParam (FALSE) when parallelising across multiple workers. progressbar logical(1) Enable progress bar (based on plyr:::progress\_text). X Any object for which methods length, [, and [[ are implemented. FUN The function to be applied to each element of X.

#### Value

Binned peaks matrix

#### **Examples**

remove\_nonstandard\_chrom

Remove non-standard chromosomes

#### **Description**

Remove non-standard chromosomes from a list of GRanges objects.

# Usage

```
remove_nonstandard_chrom(
  grlist,
  keep_chr = paste0("chr", c(seq_len(22), "X", "Y")),
  verbose = TRUE
)
```

## **Arguments**

grlist Named list of GRanges objects.
keep\_chr Which chromosomes to keep.
verbose Print messages.

50 report\_header

#### Value

Named list of GRanges objects.

report\_command

Report command

## **Description**

Reconstruct the EpiCompare command used to generate the current Rmarkdown report.

## Usage

```
report_command(params, peaklist_tidy, reference_tidy)
```

## **Arguments**

params Parameters supplied to the Rmarkdown template.

peaklist\_tidy Post-processed target peaks.

reference\_tidy Post-processed reference peaks.

#### Value

String reconstructing R function call.

## **Examples**

```
# report_command()
```

report\_header

Report header

## **Description**

Generate a header for EpiCompare reports generated using the EpiCompare.Rmd template.

## Usage

```
report_header()
```

#### Value

Header string to be rendering within Rmarkdown file.

```
report_header()
```

save\_output 51

save_output	Save output
-------------	-------------

# Description

This function saves data frames and plots generated by EpiCompare.

# Usage

```
save_output(
   save_output = FALSE,
   file,
   file_type,
   filename,
   outpath,
   interactive = FALSE,
   verbose = TRUE
)
```

# Arguments

save_output	Default FALSE. If TRUE, outputs are saved.
file	Tables and plots to be saved.
file_type	Type of file to be saved. "data.frame", "ggplot", "image"
filename	Name of file.
outpath	Outpath
interactive	Default FALSE. If TRUE, interactive plots are saved as html.
verbose	Print messages.

## Value

Saved data frames and plots.

# Description

Set the min/max values in a data.frame.

# Usage

```
set_min_max(df, colname, min_val = 0, max_val = 100)
```

52 tidy\_chromosomes

## **Arguments**

df data.frame

colname Column name to check.

min\_val Minimum value.
max\_val Maximum value.

## Value

data.frame

stopper

Stop messages

## **Description**

Conditionally print stop messages. Allows developers to easily control verbosity of functions, and meet Bioconductor requirements that dictate the stop message must first be stored to a variable before passing to stop.

## Usage

```
stopper(..., v = TRUE)
```

## **Arguments**

ν

Whether to print messages or not.

## Value

Null

tidy\_chromosomes

Remove odd chromosomes from GRanges objects

## **Description**

This convenience function removes non-standard, mitochondrial, and/or sex chromosomes from any GRanges object.

## Usage

```
tidy_chromosomes(
   gr,
   keep.X = TRUE,
   keep.Y = TRUE,
   keep.M = FALSE,
   keep.nonstandard = FALSE,
   genome = NULL
)
```

tidy\_chromosomes 53

#### **Arguments**

gr

Any GRanges object, or any another object with associated seqinfo (or a Seqinfo object itself). The object should typically have a standard genome associated with it, e.g. genome(gr) <- "hg38". gr can also be a list of such GRanges objects.

keep. X, keep. Y, keep. M, keep. nonstandard

Logicals indicating which non-autosomes should be kept. By default, sex chromosomes are kept, but mitochondrial and non-standard chromosomes are removed.

genome

An optional string that, if supplied, will be used to set the genome of gr.

#### **Details**

This function is adapted from tidyChromosomes in the BRGenomics package licensed under the Artistic License 2.0. Original author: Mike DeBerardine <a href="https://github.com/mdeber">https://github.com/mdeber</a>

Standard chromosomes are defined using the standardChromosomes function from the GenomeInfoDb package.

#### Value

A GRanges object in which both ranges and seqinfo associated with trimmed chromosomes have been removed.

#### Author(s)

Mike DeBerardine

#### See Also

GenomeInfoDb::standardChromosomes

54 translate\_genome

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tiav	peakfile	•

Tidy peakfiles in GRanges

## Description

This function filters peak files by removing peaks in blacklisted regions and in non-standard chromosomes. It also checks that the input list of peakfiles is named. If no names are provided, default file names will be used.

## Usage

```
tidy_peakfile(peaklist, blacklist)
```

### **Arguments**

peaklist A named list of peak files as GRanges object. Objects must be named and listed

using list(). e.g. list("name1"=file1, "name2"=file2) If not named, de-

fault names are assigned.

blacklist Peakfile specifying blacklisted regions as GRanges object.

#### Value

list of GRanges object

## **Examples**

translate\_genome

Translate genome

## **Description**

Translate the name of a genome build from one format to another.

tss\_plot 55

#### Usage

```
translate_genome(
  genome,
  style = c("UCSC", "Ensembl", "NCBI"),
  default_genome = NULL,
  omit_subversion = TRUE
)
```

## **Arguments**

genome A character vector of genomes equivalent to UCSC version or Ensembl Assemblies

style A single value equivalent to "UCSC" or "Ensembl" specifying the output genome default\_genome Default genome build when genome is NULL.

omit\_subversion

Omit any subversion suffixes after the ".".

#### Value

Standardized genome build name as a character string.

## **Examples**

```
genome <- translate_genome(genome="hg38", style="Ensembl")
genome2 <- translate_genome(genome="mm10", style="UCSC")</pre>
```

tss\_plot

Read count frequency around TSS

## **Description**

This function generates a plot of read count frequency around TSS.

## Usage

```
tss_plot(
  peaklist,
  txdb = NULL,
  tss_distance = c(-3000, 3000),
  conf = 0.95,
  resample = 500,
  interact = FALSE,
  workers = check_workers()
)
```

56 width\_boxplot

## **Arguments**

peaklist A list of peak files as GRanges object. Files must be listed and named using

list(). e.g. list("name1"=file1, "name2"=file2) If not named, default

file names will be assigned.

txdb A TxDb annotation object from Bioconductor.

tss\_distance A vector specifying the distance upstream and downstream around transcription

start sites (TSS). The default value is c(-3000, 3000); meaning peak frequency

3000bp upstream and downstream of TSS will be displayed.

conf Confidence interval threshold estimated by bootstrapping (0.95 means 95 Ar-

gument passed to plotAvgProf.

resample Number of bootstrapped iterations to run. Argument passed to plotAvgProf.

interact Default TRUE. By default, plots are interactive. If set FALSE, all plots in the

report will be static.

workers Number of cores to parallelise bootstrapping across. Argument passed to plotAvg-

Prof.

#### Value

A named list of profile plots.

## **Examples**

width\_boxplot

Peak width boxplot

#### **Description**

This function creates boxplots showing the distribution of widths in each peak file.

# Usage

```
width_boxplot(peaklist, interact = FALSE)
```

## Arguments

peaklist A list of peak files as GRanges object. Files must be named and listed using

list(). e.g. list("name1"=file1, "name2"=file2)

interact Default TRUE. By default, plots are interactive. If set FALSE, all plots in the

report will be static.

write\_example\_peaks 57

#### Value

A boxplot of peak widths.

## **Examples**

```
### Load Data ###
data("encode_H3K27ac") # example peaklist GRanges object
data("CnT_H3K27ac") # example peaklist GRanges object
peaklist <- list("encode"=encode_H3K27ac, "CnT"=CnT_H3K27ac)
my_plot <- width_boxplot(peaklist = peaklist)</pre>
```

write\_example\_peaks

Write example peaks

## Description

Write example peaks datasets to disk.

## Usage

```
write_example_peaks(
  dir = file.path(tempdir(), "processed_results"),
  datasets = c("encode_H3K27ac", "CnT_H3K27ac", "CnR_H3K27ac")
)
```

## Arguments

dir Directory to save peak files to.

datasets Example datasets from **EpiCompare** to write.

#### Value

Named vector of paths to saved peak files.

```
save_paths <- EpiCompare::write_example_peaks()</pre>
```

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