# Package 'ChIPpeakAnno'

July 23, 2025

# **Title** Batch annotation of the peaks identified from either ChIP-seq, ChIP-chip experiments, or any experiments that result in large number of genomic interval data Version 3.42.0 **Encoding UTF-8** Author Lihua Julie Zhu, Jianhong Ou, Jun Yu, Kai Hu, Haibo Liu, Junhui Li, Hervé Pagès, Claude Gazin. Nathan Lawson, Ryan Thompson, Simon Lin, David Lapointe, Michael Green **Maintainer** Jianhong Ou < jou@morgridge.org>, Lihua Julie Zhu <julie.zhu@umassmed.edu>, Kai Hu <kai.hu@umassmed.edu>, Junhui Li <junhui.li@umassmed.edu> **Depends** R (>= 3.5), methods, IRanges (>= 2.13.12), GenomicRanges (>= 1.31.8), S4Vectors (>= 0.17.25) **Imports** AnnotationDbi, BiocGenerics (>= 0.1.0), Biostrings (>= 2.47.6), pwalign, DBI, dplyr, GenomeInfoDb, GenomicAlignments, GenomicFeatures, RBGL, Rsamtools, SummarizedExperiment, VennDiagram, biomaRt, ggplot2, grDevices, graph, graphics, grid, InteractionSet, KEGGREST, matrixStats, multtest, regioneR, rtracklayer, stats, utils, universalmotif, stringr, tibble, tidyr, data.table, scales, ensembldb Suggests AnnotationHub, BSgenome, limma, reactome.db, BiocManager,

BiocStyle, BSgenome. Ecoli. NCBI. 20080805,

Type Package

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BSgenome.Hsapiens.UCSC.hg19, org.Ce.eg.db, org.Hs.eg.db, BSgenome.Celegans.UCSC.ce10, BSgenome.Drerio.UCSC.danRer7, BSgenome.Hsapiens.UCSC.hg38, DelayedArray, idr, seqinr, EnsDb.Hsapiens.v75, EnsDb.Hsapiens.v79, EnsDb.Hsapiens.v86, TxDb.Hsapiens.UCSC.hg18.knownGene, TxDb.Hsapiens.UCSC.hg19.knownGene, TxDb.Hsapiens.UCSC.hg38.knownGene, GO.db, gplots, UpSetR, knitr, rmarkdown, reshape2, testthat, trackViewer, motifStack, OrganismDbi, BiocFileCache

Description The package encompasses a range of functions for identifying the closest gene, exon, miRNA, or custom features—such as highly conserved elements and user-supplied transcription factor binding sites.

Additionally, users can retrieve sequences around the peaks and obtain enriched Gene Ontology (GO) or Pathway terms. In version 2.0.5 and beyond, new functionalities have been introduced. These include features for identifying peaks associated with bi-directional promoters along with summary statistics (peaksNearBDP), summarizing motif occurrences in peaks (summarizePatternInPeaks), and associating additional identifiers with annotated peaks or enrichedGO (addGeneIDs). The package integrates with various other packages such as biomaRt, IRanges, Biostrings, BSgenome, GO.db, multtest, and stat to enhance its analytical capabilities.

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LazyData true
LazyDataCompression xz
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VignetteBuilder knitr
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# Description

The package includes functions to retrieve the sequences around the peak, obtain enriched Gene Ontology (GO) terms, find the nearest gene, exon, miRNA or custom features such as most conserved elements and other transcription factor binding sites leveraging biomaRt, IRanges, Biostrings, BSgenome, GO.db, hypergeometric test phyper and multtest package.

#### **Details**

Package: ChIPpeakAnno

Type: Package
Version: 3.0.0
Date: 2014-10-24
License: LGPL
LazyLoad: yes

### Author(s)

Lihua Julie Zhu, Jianhong Ou, Hervé Pagès, Claude Gazin, Nathan Lawson, Simon Lin, David Lapointe and Michael Green

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#### References

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- 7. S. Holm (1979). A simple sequentially rejective multiple test procedure. Scand. J. Statist.. Vol. 6: 65-70.
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- 9. Zhu L.J. et al. (2010) ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIP-chip data. BMC Bioinformatics 2010, 11:237doi:10.1186/1471-2105-11-237.

```
if(interactive()){
  data(myPeakList)
  library(ensembldb)
  library(EnsDb.Hsapiens.v75)
  anno <- annoGR(EnsDb.Hsapiens.v75)
  annotatedPeak <-
     annotatePeakInBatch(myPeakList[1:6], AnnotationData=anno)</pre>
```

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}

addAncestors

Add GO IDs of the ancestors for a given vector of GO ids

# Description

Add GO IDs of the ancestors for a given vector of GO IDs leveraging GO.db

# Usage

```
addAncestors(go.ids, ontology = c("bp", "cc", "mf"))
```

# **Arguments**

go.ids A matrix with 4 columns: first column is GO IDs and 4th column is entrez IDs.

ontology bp for biological process, cc for cellular component and mf for molecular func-

tion.

### Value

A vector of GO IDs containing the input GO IDs with the GO IDs of their ancestors added.

# Author(s)

Lihua Julie Zhu

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addGeneIDs	Add common IDs to annotated peaks such as gene symbol, entrez ID,
	ensemble gene id and refseq id.

#### **Description**

Add common IDs to annotated peaks such as gene symbol, entrez ID, ensemble gene id and refseq id leveraging organism annotation dataset. For example, org.Hs.eg.db is the dataset from orgs.Hs.eg.db package for human, while org.Mm.eg.db is the dataset from the org.Mm.eg.db package for mouse.

# Usage

```
addGeneIDs(
  annotatedPeak,
  orgAnn,
  IDs2Add = c("symbol"),
  feature_id_type = "ensembl_gene_id",
  silence = TRUE,
  mart
)
```

### **Arguments**

```
annotatedPeak GRanges or a vector of feature IDs.

orgAnn organism annotation dataset such as org.Hs.eg.db.

IDs2Add a vector of annotation identifiers to be added feature_id_type type of ID to be annotated, default is ensembl_gene_id

silence TRUE or FALSE. If TRUE, will not show unmapped entrez id for feature ids.

mart object, see useMart of biomaRt package for details
```

# Details

One of orgAnn and mart should be assigned.

• If orgAnn is given, parameter feature\_id\_type should be ensemble\_gene\_id, entrez\_id, gene\_symbol, gene\_alias or refseq\_id. And parameter IDs2Add can be set to any combination of identifiers such as "accnum", "ensembl", "ensemblprot", "ensembltrans", "entrez\_id", "enzyme", "genename", "pfam", "pmid", "prosite", "refseq", "symbol", "unigene" and "uniprot". Some IDs are unique to an organism, such as "omim" for org.Hs.eg.db and "mgi" for org.Mm.eg.db.

Here is the definition of different IDs:

- accnum: GenBank accession numbers
- ensembl: Ensembl gene accession numbers
- ensemblprot: Ensembl protein accession numbers

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- ensembltrans: Ensembl transcript accession numbers

- entrez\_id: entrez gene identifiers

enzyme: EC numbers
genename: gene name
pfam: Pfam identifiers
pmid: PubMed identifiers
prosite: PROSITE identifiers
refseq: RefSeq identifiers
symbol: gene abbreviations

unigene: UniGene cluster identifiersuniprot: Uniprot accession numbers

- omim: OMIM(Mendelian Inheritance in Man) identifiers

- mgi: Jackson Laboratory MGI gene accession numbers

• If mart is used instead of orgAnn, for valid parameter feature\_id\_type and IDs2Add parameters, please refer to getBM in bioMart package. Parameter feature\_id\_type should be one valid filter name listed by listFilters(mart) such as ensemble\_gene\_id. And parameter IDs2Add should be one or more valid attributes name listed by listAttributes(mart) such as external\_gene\_id, entrezgene, wikigene\_name, or mirbase\_transcript\_name.

#### Value

GRanges if the input is a GRanges or dataframe if input is a vector.

### Author(s)

Jianhong Ou, Lihua Julie Zhu

### References

http://www.bioconductor.org/packages/release/data/annotation/

### See Also

```
getBM, AnnotationDb
```

addMetadata 9

```
IDs2Add=c("hgnc_symbol","entrezgene"))
}
```

addMetadata

Add metadata of the GRanges objects used for findOverlapsOfPeaks

### **Description**

Add metadata to to overlapping peaks after calling findOverlapsOfPeaks.

### Usage

```
addMetadata(ol, colNames = NULL, FUN = c, ...)
```

# **Arguments**

ol An object of overlappingPeaks, which is output of findOverlapsOfPeaks.

colNames Names of metadata column to be added. If it is NULL, addMetadata will guess

what to add.

FUN A function to be called

... Arguments to the function call.

# Value

return value is An object of overlappingPeaks.

### Author(s)

Jianhong Ou

### See Also

See Also as findOverlapsOfPeaks

10 annoGR-class

```
ol <- findOverlapsOfPeaks(peaks1, peaks2)
addMetadata(ol)</pre>
```

annoGR-class

Class annoGR

# **Description**

An object of class annoGR represents the annotation data could be used by annotationPeakInBatch.

# Usage

```
## S4 method for signature 'annoGR'
info(object)
## S4 method for signature 'GRanges'
annoGR(ranges, feature = "group", date, ...)
## S4 method for signature 'TxDb'
annoGR(
  ranges,
 feature = c("gene", "transcript", "exon", "CDS", "fiveUTR", "threeUTR", "microRNA",
    "tRNAs", "geneModel"),
  date,
  source,
 mdata,
  OrganismDb
## S4 method for signature 'EnsDb'
annoGR(
  ranges,
  feature = c("gene", "transcript", "exon", "disjointExons"),
  date,
  source,
 mdata
)
```

# Arguments

```
object annoGR object.

ranges an object of GRanges, TxDb or EnsDb

feature annotation type

date a Date object

... could be following parameters
```

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source character, where the annotation comes from

mdata data frame, metadata from annotation

OrganismDb an object of OrganismDb. It is used for extracting gene symbol for geneModel

group for TxDb

### **Slots**

seqnames, ranges, strand, elementMetadata, seqinfo slots inherit from GRanges. The ranges must have unique names.

source character, where the annotation comes from

```
date a Date object
```

feature annotation type, could be "gene", "exon", "transcript", "CDS", "fiveUTR", "threeUTR", "microRNA", "tRNAs", "geneModel" for TxDb object, or "gene", "exon", "transcript" for EnsDb object

mdata data frame, metadata from annotation

# **Objects from the Class**

Objects can be created by calls of the form new("annoGR", date, elementMetadata, feature, mdata, ranges, seqinfo, seqnames, source, strand)

# Author(s)

Jianhong Ou

### **Examples**

```
if(interactive() || Sys.getenv("USER")=="jianhongou"){
   library(EnsDb.Hsapiens.v79)
   anno <- annoGR(EnsDb.Hsapiens.v79)
}</pre>
```

annoPeaks

Annotate peaks

# **Description**

Annotate peaks by annoGR object in the given range.

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### Usage

```
annoPeaks(
  peaks,
  annoData,
  bindingType = c("nearestBiDirectionalPromoters", "startSite", "endSite", "fullRange"),
  bindingRegion = c(-5000, 5000),
  ignore.peak.strand = TRUE,
  select = c("all", "bestOne"),
  ...
)
```

### **Arguments**

peaks peak list, GRanges object

annoData annotation data, GRanges object

bindingType

Specifying the criteria to associate peaks with annotation. Here is how to use it together with the parameter bindingRegion

- To obtain peaks within 5kb upstream and up to 3kb downstream of TSS within the gene body, set bindingType = "startSite" and bindingRegion = c(-5000, 3000)
- To obtain peaks up to 5kb upstream within the gene body and 3kb downstream of gene/Exon End, set bindingType = "endSite" and bindingRegion = c(-5000, 3000)
- To obtain peaks from 5kb upstream to 3kb downstream of genes/Exons, set bindingType = "fullRange" and bindingRegion = c(-5000, 3000)
- To obtain peaks with nearest bi-directional promoters within 5kb upstream and 3kb downstream of TSS, set bindingType = "nearestBiDirectionalPromoters" and bindingRegion = c(-5000, 3000)

startSite start position of the feature (strand is considered)

endSite end position of the feature (strand is considered)

fullRange whole range of the feature

**nearestBiDirectionalPromoters** nearest promoters from both direction of the peaks (strand is considered). It will report bidirectional promoters if there are promoters in both directions in the given region (defined by bindingRegion). Otherwise, it will report the closest promoter in one direction.

bindingRegion

Annotation range used together with binding Type, which is a vector with two integer values, default to c (-5000, 5000). The first one must be no bigger than 0, which means upstream. And the sec ond one must be no less than 1, which means downstream (1 is the site position, 2 is the next base of the site position). For details, see binding Type.

ignore.peak.strand

ignore the peaks strand or not.

select

"all" or "bestOne". Return the annotation containing all or the best one. The "bestOne" is selected by the shortest distance to the sites and then similarity between peak and annotations. Ignored if bindingType is nearestBiDirectional-Promoters.

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... Not used.

#### Value

Output is a GRanges object of the annotated peaks.

### Author(s)

Jianhong Ou

#### See Also

See Also as annotatePeakInBatch

#### **Examples**

```
library(ensembldb)
library(EnsDb.Hsapiens.v75)
data("myPeakList")
annoGR <- toGRanges(EnsDb.Hsapiens.v75)
seqlevelsStyle(myPeakList) <- seqlevelsStyle(annoGR)
annoPeaks(myPeakList, annoGR)</pre>
```

annotatedPeak

Annotated Peaks

# **Description**

TSS annotated putative STAT1-binding regions that are identified in un-stimulated cells using ChIP-seq technology (Robertson et al., 2007)

### Usage

annotatedPeak

#### **Format**

GRanges with slot start holding the start position of the peak, slot end holding the end position of the peak, slot names holding the id of the peak, slot strand holding the strands and slot space holding the chromosome location where the peak is located. In addition, the following variables are included.

list("feature") id of the feature such as ensembl gene ID

**list("insideFeature")** upstream: peak resides upstream of the feature; downstream: peak resides downstream of the feature; inside: peak resides inside the feature; overlapStart: peak overlaps with the start of the feature; overlapEnd: peak overlaps with the end of the feature; include-Feature: peak include the feature entirely

list("distancetoFeature") distance to the nearest feature such as transcription start site

```
list("start_position") start position of the feature such as gene
list("end_position") end position of the feature such as the gene
```

#### **Details**

```
obtained by data(TSS.human.GRCh37)
data(myPeakList)
annotatePeakInBatch(myPeakList, AnnotationData = TSS.human.GRCh37, output="b", multiple=F)
```

# **Examples**

annotatePeakInBatch

Obtain the distance to the nearest TSS, miRNA, and/or exon for a list of peaks

### **Description**

Obtain the distance to the nearest TSS, miRNA, exon et al for a list of peak locations leveraging IRanges and biomaRt package

### Usage

```
annotatePeakInBatch(
   myPeakList,
   mart,
   featureType = c("TSS", "miRNA", "Exon"),
   AnnotationData,
   output = c("nearestLocation", "overlapping", "both", "shortestDistance", "inside",
        "upstream&inside", "inside&downstream", "upstream", "downstream",
        "upstreamORdownstream", "nearestBiDirectionalPromoters"),
   multiple = c(TRUE, FALSE),
   maxgap = -1L,
   PeakLocForDistance = c("start", "middle", "end", "endMinusStart"),
   FeatureLocForDistance = c("TSS", "middle", "start", "end", "geneEnd"),
   select = c("all", "first", "last", "arbitrary"),
   ignore.strand = TRUE,
```

```
bindingRegion = NULL,
...
)
```

#### **Arguments**

myPeakList A GRanges object

mart A mart object, used if AnnotationData is not supplied, see useMart of bioMaRt

package for details

featureType A charcter vector used with mart argument if AnnotationData is not supplied;

choose from "TSS", "miRNA" or "Exon"

AnnotationData A GRanges or annoGR object. It can be obtained from the function getAnnota-

tion or customized annotation of class GRanges containing additional variable: strand (1 or + for plus strand and -1 or - for minus strand). Pre-complied annotations, such as TSS.human.NCBI36, TSS.mouse.NCBIM37, TSS.rat.RGSC3.4 and TSS.zebrafish.Zv8, are provided by this package (attach them with data() function). Another method to provide annotation data is to obtain through biomaRt

in real time by using the mart and feature Type option

nearestLocation (default) will output the nearest features calculated as Peak-Loc - FeatureLocForDistance; when selected, the output can consist of both "strictly nearest features (non-overlapping)" and "overlapping features" as

long as they are the nearest

**overlapping** will output overlapping features with maximum gap specified as maxgap between peak range and feature range; it is possible for a peak to be annotated with zero ("NA" will be returned) or multiple overlapping features if exist

**both** will output all the nearest features as well as any features that overlap with the peak that is not the nearest

**shortestDistance** will output the features with the shortest distance; the "shortest distance" is determined from either ends of the feature to either ends of the peak

**upstream&inside** will output all upstream and overlapping features with maximum gap

inside&downstream will output all downstream and overlapping features with maximum gap

upstream will output all upstream features with maximum gap

downstream will output all downstream features with maximum gap

**upstreamORdownstream** will output all upstream features with maximum gap or downstream with maximum gap

**nearestBiDirectionalPromoters** will use annoPeaks to annotate peaks. Nearest promoters from both direction of the peaks (strand is considered). It will report bidirectional promoters if there are promoters in both directions in the given region (defined by bindingRegion). Otherwise, it will report the closest promoter in one direction.

multiple

Not applicable when output is nearest. TRUE: output multiple overlapping features for each peak. FALSE: output at most one overlapping feature for each peak. This parameter is kept for backward compatibility, please use select.

output

maxgap

The maximum gap that is allowed between 2 ranges for the ranges to be considered as overlapping. The gap between 2 ranges is the number of positions that separate them. The gap between 2 adjacent ranges is 0. By convention when one range has its start or end strictly inside the other (i.e. non-disjoint ranges), the gap is considered to be -1.

#### PeakLocForDistance

Specify the location of peak for calculating distance, i.e., middle means using middle of the peak to calculate distance to feature, start means using start of the peak to calculate the distance to feature, endMinusStart means using the end of the peak to calculate the distance to features on plus strand and the start of the peak to calculate the distance to features on minus strand. To be compatible with previous version, by default using start

#### FeatureLocForDistance

Specify the location of feature for calculating distance, i.e., middle means using middle of the feature to calculate distance of peak to feature, start means using start of the feature to calculate the distance to feature, TSS means using start of feature when feature is on plus strand and using end of feature when feature is on minus strand, geneEnd means using end of feature when feature is on plus strand and using start of feature when feature is on minus strand. To be compatible with previous version, by default using TSS

"all" may return multiple overlapping peaks, "first" will return the first overlapping peak, "last" will return the last overlapping peak and "arbitrary" will return one of the overlapping peaks.

ignore.strand

When set to TRUE, the strand information is ignored in the annotation. Unless you have stranded peaks and you are interested in annotating peaks to the features in the same strand only, you should just use the default setting ignore.strand = TRUE.

Annotation range used for annoPeaks, which is a vector with two integer values, default to c (-5000, 5000). The first one must be no bigger than 0. And the sec ond one must be no less than 1. Once bindingRegion is defined, annotation will based on annoPeaks. Here is how to use it together with the parameter output and FeatureLocForDistance.

- To obtain peaks with nearest bi-directional promoters within 5kb upstream and 3kb downstream of TSS, set output = "nearestBiDirectionalPromoters" and bindingRegion = c(-5000, 3000)
- To obtain peaks within 5kb upstream and up to 3kb downstream of TSS within the gene body, set output="overlapping", FeatureLocForDistance="TSS" and bindingRegion = c(-5000, 3000)
- To obtain peaks up to 5kb upstream within the gene body and 3kb downstream of gene/Exon End, set output="overlapping", FeatureLocForDistance="geneEnd" and bindingRegion = c(-5000, 3000)
- To obtain peaks from 5kb upstream to 3kb downstream of genes/Exons, set output="overlapping", bindingType = "fullRange" and bindingRegion = c(-5000, 3000)

For details, see annoPeaks.

Parameters could be passed to annoPeaks

select

bindingRegion

#### Value

An object of GRanges with slot start holding the start position of the peak, slot end holding the end position of the peak, slot space holding the chromosome location where the peak is located, slot rownames holding the id of the peak. In addition, the following variables are included.

list("feature")

id of the feature such as ensembl gene ID

list("insideFeature")

upstream: peak resides upstream of the feature; downstream: peak resides downstream of the feature; inside: peak resides inside the feature; overlapStart: peak overlaps with the start of the feature; overlapEnd: peak overlaps with the end of the feature; includeFeature: peak include the feature entirely

list("distancetoFeature")

distance to the nearest feature such as transcription start site. By default, the distance is calculated as the distance between the start of the binding site and the TSS that is the gene start for genes located on the forward strand and the gene end for genes located on the reverse strand. The user can specify the location of peak and location of feature for calculating this

list("start\_position")

start position of the feature such as gene

list("end\_position")

end position of the feature such as the gene

list("strand") 1 or + for positive strand and -1 or - for negative strand where the feature is located

list("shortestDistance")

The shortest distance from either end of peak to either end the feature.

list("fromOverlappingOrNearest")

Relevant only when output is set to "both". If "nearestLocation": indicates this feature's start (feature's end for features from minus strand) is the closest to the peak start ("strictly nearest" or "nearest overlapping"); if "Overlapping": indicates this feature overlaps with this peak although it is not the nearest (non-nearest overlapping)

### Author(s)

Lihua Julie Zhu, Jianhong Ou

#### References

- 1. Zhu L.J. et al. (2010) ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIP-chip data. BMC Bioinformatics 2010, 11:237doi:10.1186/1471-2105-11-237
- 2. Zhu L (2013). "Integrative analysis of ChIP-chip and ChIP-seq dataset." In Lee T and Luk ACS (eds.), Tilling Arrays, volume 1067, chapter 4, pp. -19. Humana Press. http://dx.doi.org/10.1007/978-1-62703-607-8\_8

#### See Also

getAnnotation, findOverlappingPeaks, makeVennDiagram, addGeneIDs, peaksNearBDP, summarizePatternInPeaks, annoGR, annoPeaks

```
## example 1: annotate myPeakList by TxDb or EnsDb.
data(myPeakList)
library(ensembldb)
library(EnsDb.Hsapiens.v75)
annoData <- annoGR(EnsDb.Hsapiens.v75)</pre>
annotatePeak = annotatePeakInBatch(myPeakList[1:6], AnnotationData=annoData)
annotatePeak
## example 2: annotate myPeakList (GRanges)
## with TSS.human.NCBI36 (Granges)
data(TSS.human.NCBI36)
annotatedPeak = annotatePeakInBatch(myPeakList[1:6],
                                    AnnotationData=TSS.human.NCBI36)
annotatedPeak
## example 3: you have a list of transcription factor biding sites from
## literature and are interested in determining the extent of the overlap
## to the list of peaks from your experiment. Prior calling the function
## annotatePeakInBatch, need to represent both dataset as GRanges
## where start is the start of the binding site, end is the end of the
## binding site, names is the name of the binding site, space and strand
## are the chromosome name and strand where the binding site is located.
myexp <- GRanges(segnames=c(6,6,6,6,6,5,4,4),
                 IRanges(start=c(1543200,1557200,1563000,1569800,
                                 167889600,100,1000),
                         end=c(1555199,1560599,1565199,1573799,
                               167893599,200,1200),
                         names=c("p1","p2","p3","p4","p5","p6", "p7")),
                 strand="+")
literature <- GRanges(seqnames=c(6,6,6,6,6,5,4,4),
                      IRanges(start=c(1549800,1554400,1565000,1569400,
                                       167888600,120,800),
                              end=c(1550599,1560799,1565399,1571199,
                                    167888999,140,1400),
                              names=c("f1","f2","f3","f4","f5","f6","f7")),
                      strand=rep(c("+", "-"), c(5, 2)))
annotatedPeak1 <- annotatePeakInBatch(myexp,</pre>
                                      AnnotationData=literature)
pie(table(annotatedPeak1$insideFeature))
annotatedPeak1
### use toGRanges or rtracklayer::import to convert BED or GFF format
### to GRanges before calling annotatePeakInBatch
test.bed <- data.frame(space=c("4", "6"),</pre>
                       start=c("100", "1000"),
                       end=c("200", "1100"),
                       name=c("peak1", "peak2"))
test.GR = toGRanges(test.bed)
annotatePeakInBatch(test.GR, AnnotationData = literature)
```

```
library(testthat)
peak <- GRanges(segnames = "chr1",</pre>
                 IRanges(start = 24736757, end=24737528,
                         names = "testPeak"))
data(TSS.human.GRCh37)
TSS.human.GRCh37[names(TSS.human.GRCh37) == "ENSG00000001461"]
# GRanges object with 1 range and 1 metadata column:
                       ranges strand |
                                                   description
#<Rle>
                <IRanges> <Rle> |
                                               <character>
# ENSG00000001461
                         1 24742285-24799466
                                                   + | NIPA-like domain con..
#GRanges object with 1 range and 0 metadata columns:
   segnames
                        ranges strand
                <IRanges> <Rle>
#<Rle>
# testPeak
                 chr1 24736757-24737528
TSS.human.GRCh37[names(TSS.human.GRCh37)== "ENSG00000001460"]
#GRanges object with 1 range and 1 metadata column:
    seqnames
                         ranges strand |
                                                    description
#<Rle>
                <IRanges> <Rle> |
                                               <character>
    ENSG00000001460
                            1 24683490-24743424
                                                     - | UPF0490 protein Clor..
ap <- annotatePeakInBatch(peak, Annotation=TSS.human.GRCh37,</pre>
                           PeakLocForDistance = "start")
stopifnot(ap$feature=="ENSG00000001461")
ap <- annotatePeakInBatch(peak, Annotation=TSS.human.GRCh37,</pre>
                           PeakLocForDistance = "end")
 stopifnot(ap$feature=="ENSG00000001461")
ap <- annotatePeakInBatch(peak, Annotation=TSS.human.GRCh37,</pre>
                           PeakLocForDistance = "middle")
stopifnot(ap$feature=="ENSG00000001461")
ap <- annotatePeakInBatch(peak, Annotation=TSS.human.GRCh37,</pre>
                           PeakLocForDistance = "endMinusStart")
stopifnot(ap$feature=="ENSG00000001461")
## Let's calculate the distances between the peak and the TSS of the genes
## in the annotation file used for annotating the peaks.
## Please note that we need to compute the distance using the annotation
## file TSS.human.GRCh37.
## If you would like to use TxDb.Hsapiens.UCSC.hg19.knownGene,
## then you will need to annotate the peaks
## using TxDb.Hsapiens.UCSC.hg19.knownGene as well.
### using start
start(peak) -start(TSS.human.GRCh37[names(TSS.human.GRCh37)==
                                     "ENSG00000001461"]) #picked
#F17 -5528
start(peak) -end(TSS.human.GRCh37[names(TSS.human.GRCh37)==
                                  "ENSG00000001460"])
#[1] -6667
#### using middle
 (start(peak) + end(peak))/2 -
     start(TSS.human.GRCh37[names(TSS.human.GRCh37)== "ENSG00000001461"])
#[1] -5142.5
 (start(peak) + end(peak))/2 -
     end(TSS.human.GRCh37[names(TSS.human.GRCh37)== "ENSG00000001460"])
 # [1] 49480566
```

```
end(peak) -start(TSS.human.GRCh37[names(TSS.human.GRCh37)==
                                  "ENSG00000001461"]) #picked
# [1] -4757
end(peak) -end(TSS.human.GRCh37[names(TSS.human.GRCh37)==
                               "ENSG00000001460"])
# [1] -5896
#### using endMinusStart
end(peak) - start(TSS.human.GRCh37[names(TSS.human.GRCh37)==
                                  "ENSG00000001461"]) ## picked
# [1] -4575
start(peak) -end(TSS.human.GRCh37[names(TSS.human.GRCh37)==
                                  "ENSG00000001460"])
#[1] -6667
##### using txdb object to annotate the peaks
library(org.Hs.eg.db)
select(org.Hs.eg.db, key="STPG1", keytype="SYMBOL",
       columns=c("ENSEMBL", "ENTREZID", "SYMBOL"))
# SYMBOL
                  ENSEMBL ENTREZID
# STPG1 ENSG00000001460
                            90529
select(org.Hs.eg.db, key= "ENSG00000001461", keytype="ENSEMBL",
       columns=c("ENSEMBL", "ENTREZID", "SYMBOL"))
#ENSEMBL ENTREZID SYMBOL
# ENSG00000001461
                     57185 NIPAL3
require(TxDb.Hsapiens.UCSC.hg19.knownGene)
txdb.ann <- genes(TxDb.Hsapiens.UCSC.hg19.knownGene)</pre>
STPG1 <- select(org.Hs.eg.db, key="STPG1", keytype="SYMBOL",</pre>
                columns=c( "SYMBOL", "ENSEMBL", "ENTREZID"))[1,3]
NIPAL3 <- select(org.Hs.eg.db, key="NIPAL3", keytype="SYMBOL",
                 columns=c( "SYMBOL", "ENSEMBL", "ENTREZID"))[1,3]
ap <- annotatePeakInBatch(peak, Annotation=txdb.ann,</pre>
                          PeakLocForDistance = "start")
expect_equal(ap$feature, STPG1)
ap <- annotatePeakInBatch(peak, Annotation=txdb.ann,</pre>
                          PeakLocForDistance = "end")
expect_equal(ap$feature, STPG1)
ap <- annotatePeakInBatch(peak, Annotation=txdb.ann,</pre>
                          PeakLocForDistance = "middle")
expect_equal(ap$feature, STPG1)
ap <- annotatePeakInBatch(peak, Annotation=txdb.ann,</pre>
                          PeakLocForDistance = "endMinusStart")
expect_equal(ap$feature, NIPAL3)
txdb.ann[NIPAL3]
txdb.ann[txdb.ann$gene_id == NIPAL3]
  GRanges object with 1 range and 1 metadata column:
     seqnames
                         ranges strand |
#
 <Rle>
                 <IRanges> <Rle> | <character>
   57185
              chr1 24742245-24799473
                                                     57185
                                          + |
#----
txdb.ann[txdb.ann$gene_id == STPG1]
    GRanges object with 1 range and 1 metadata column:
      seanames
                          ranges strand |
                                              gene_id
# <Rle>
                 <IRanges> <Rle> | <character>
      90529
                chr1 24683489-24741587
                                                       90529
```

 $assign {\tt ChromosomeRegion}$ 

Summarize peak distribution over exon, intron, enhancer, proximal promoter, 5 prime UTR and 3 prime UTR

# Description

Summarize peak distribution over exon, intron, enhancer, proximal promoter, 5 prime UTR and 3 prime UTR  $\,$ 

# Usage

```
assignChromosomeRegion(
  peaks.RD,
  exon,
  TSS,
  utr5,
  utr3,
  proximal.promoter.cutoff = c(upstream = 2000, downstream = 100),
  immediate.downstream.cutoff = c(upstream = 0, downstream = 1000),
  nucleotideLevel = FALSE,
  precedence = NULL,
  TxDb = NULL
)
```

### **Arguments**

peaks.RD	peaks in GRanges: See example below
exon	exon data obtained from getAnnotation or customized annotation of class GRanges containing additional variable: strand (1 or + for plus strand and -1 or - for minus strand). This parameter is for backward compatibility only. TxDb should be used instead.
TSS	TSS data obtained from getAnnotation or customized annotation of class GRanges containing additional variable: strand (1 or + for plus strand and -1 or - for minus strand). For example, data(TSS.human.NCBI36),data(TSS.mouse.NCBIM37), data(TSS.rat.RGSC3.4) and data(TSS.zebrafish.Zv8). This parameter is for backward compatibility only. TxDb should be used instead.
utr5	5 prime UTR data obtained from getAnnotation or customized annotation of class GRanges containing additional variable: strand (1 or + for plus strand and -1 or - for minus strand). This parameter is for backward compatibility only. TxDb should be used instead.
utr3	3 prime UTR data obtained from getAnnotation or customized annotation of class GRanges containing additional variable: strand (1 or + for plus strand and -1 or - for minus strand). This parameter is for backward compatibility only. TxDb should be used instead.

proximal.promoter.cutoff

Specify the cutoff in bases to classify proximal promoter or enhencer. Peaks that reside within proximal.promoter.cutoff upstream from or overlap with transcription start site are classified as proximal promoters. Peaks that reside upstream of the proximal.promoter.cutoff from gene start are classified as enhancers. The default is upstream 2000 bases and downstream 100 bases.

immediate.downstream.cutoff

Specify the cutoff in bases to classify immediate downstream region or enhancer region. Peaks that reside within immediate.downstream.cutoff downstream of gene end but not overlap 3 prime UTR are classified as immediate downstream. Peaks that reside downstream over immediate.downstreatm.cutoff from gene end are classified as enhancers. The default is upstream 0 bases and downstream 1000 bases.

nucleotideLevel

Logical. Choose between peak centric and nucleotide centric view. Default=FALSE

precedence

If no precedence specified, double count will be enabled, which means that if a peak overlap with both promoter and 5'UTR, both promoter and 5'UTR will be incremented. If a precedence order is specified, for example, if promoter is specified before 5'UTR, then only promoter will be incremented for the same example. The values could be any conbinations of "Promoters", "immediateDownstream", "fiveUTRs", "threeUTRs", "Exons" and "Introns", Default=NULL

TxDb an object of TxDb or similar including EnsDb

### Value

A list of two named vectors: percentage and jaccard (Jaccard Index). The information in the vectors:

list("Exons") Percent or the picard index of the peaks resided in exon regions.
list("Introns")

Percent or the picard index of the peaks resided in intron regions.

list("fiveUTRs")

Percent or the picard index of the peaks resided in 5 prime UTR regions.

list("threeUTRs")

Percent or the picard index of the peaks resided in 3 prime UTR regions.

list("Promoter")

Percent or the picard index of the peaks resided in proximal promoter regions.

list("ImmediateDownstream")

Percent or the picard index of the peaks resided in immediate downstream regions.

list("Intergenic.Region")

Percent or the picard index of the peaks resided in intergenic regions.

The Jaccard index, also known as Intersection over Union. The Jaccard index is between 0 and 1. The higher the index, the more significant the overlap between the peak region and the genomic features in consideration.

# Author(s)

Jianhong Ou, Lihua Julie Zhu

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### References

- 1. Zhu L.J. et al. (2010) ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIP-chip data. BMC Bioinformatics 2010, 11:237doi:10.1186/1471-2105-11-237
- 2. Zhu L.J. (2013) Integrative analysis of ChIP-chip and ChIP-seq dataset. Methods Mol Biol. 2013;1067:105-24. doi: 10.1007/978-1-62703-607-8\_8.

#### See Also

genomicElementDistribution, genomicElementUpSetR, binOverFeature, binOverGene, binOverRegions

### **Examples**

```
if (interactive() || Sys.getenv("USER")=="jianhongou"){
    ##Display the list of genomes available at UCSC:
    #library(rtracklayer)
    #ucscGenomes()[, "db"]
    ## Display the list of Tracks supported by makeTxDbFromUCSC()
    #supportedUCSCtables()
    ##Retrieving a full transcript dataset for Human from UCSC
    ##TranscriptDb <-
           makeTxDbFromUCSC(genome="hg19", tablename="ensGene")
    if(require(TxDb.Hsapiens.UCSC.hg19.knownGene)){
      TxDb <- TxDb.Hsapiens.UCSC.hg19.knownGene
      exons <- exons(TxDb, columns=NULL)</pre>
      fiveUTRs <- unique(unlist(fiveUTRsByTranscript(TxDb)))</pre>
      Feature.distribution <-
          assign Chromosome Region (exons, nucleotide Level = TRUE, TxDb = TxDb) \\
      barplot(Feature.distribution$percentage)
      assignChromosomeRegion(fiveUTRs, nucleotideLevel=FALSE, TxDb=TxDb)
      data(myPeakList)
      assignChromosomeRegion(myPeakList, nucleotideLevel=TRUE,
                              precedence=c("Promoters", "immediateDownstream",
                                           "fiveUTRs", "threeUTRs",
                                           "Exons", "Introns"),
                              TxDb=TxDb)
}
```

bdp

obtain the peaks near bi-directional promoters

### **Description**

Obtain the peaks near bi-directional promoters. Also output percent of peaks near bi-directional promoters.

24 bindist-class

### Usage

```
bdp(peaks, annoData, maxgap = 2000L, ...)
```

### **Arguments**

```
peaks peak list, GRanges object
annoData annotation data, annoGR object
maxgap maxgap between peak and TSS
... Not used.
```

#### Value

Output is a list of GRanges object of the peaks near bi-directional promoters.

### Author(s)

Jianhong Ou

### See Also

See Also as annoPeaks, annoGR

# **Examples**

```
if(interactive() || Sys.getenv("USER")=="jianhongou"){
  library(ensembldb)
  library(EnsDb.Hsapiens.v75)
  data("myPeakList")
  annoGR <- annoGR(EnsDb.Hsapiens.v75)
  seqlevelsStyle(myPeakList) <- seqlevelsStyle(annoGR)
  ChIPpeakAnno:::bdp(myPeakList, annoGR)
}</pre>
```

bindist-class

Class "bindist"

### **Description**

An object of class "bindist" represents the relevant fixed-width range of binding site from the feature and number of possible binding site in each range.

### **Objects from the Class**

Objects can be created by calls of the form new("bindist", counts="integer", mids="integer", halfBinSize="integer" bindingType="character", featureType="character").

binOverFeature 25

### See Also

preparePool, peakPermTest

binOverFeature

Aggregate peaks over bins from the TSS

# **Description**

Aggregate peaks over bins from the feature sites.

# Usage

```
binOverFeature(
  annotationData = GRanges(),
  select = c("all", "nearest"),
  radius = 5000L,
 nbins = 50L,
 minGeneLen = 1L,
 aroundGene = FALSE,
 mbins = nbins,
  featureSite = c("FeatureStart", "FeatureEnd", "bothEnd"),
 PeakLocForDistance = c("all", "end", "start", "middle"),
  FUN = sum,
  errFun = sd,
  xlab,
 ylab,
 main
)
```

# **Arguments**

 Objects of	GRanges to	be analyzed

annotationData An object of GRanges or annoGR for annotation

select Logical: annotate the peaks to all features or the nearest one

radius The radius of the longest distance to feature site

nbins The number of bins

minGeneLen The minimal gene length

aroundGene Logical: count peaks around features or a given site of the features. Default =

**FALSE** 

mbins if aroundGene set as TRUE, the number of bins intra-feature. The value will be

normalized by value \* (radius/genelen) \* (mbins/nbins)

featureSite which site of features should be used for distance calculation

26 binOverGene

#### PeakLocForDistance

which site of peaks should be used for distance calculation

FUN the function to be used for score calculation

errFun the function to be used for errorbar calculation or values for the errorbar.

xlab titles for each x axis
ylab titles for each y axis
main overall titles for each plot

### Value

A data.frame with bin values.

### Author(s)

Jianhong Ou

# **Examples**

binOverGene

coverage of gene body

### **Description**

calculate the coverage of gene body per gene per bin.

# Usage

```
binOverGene(
   cvglists,
   TxDb,
   upstream.cutoff = 0L,
   downstream.cutoff = upstream.cutoff,
   nbinsGene = 100L,
   nbinsUpstream = 20L,
   nbinsDownstream = nbinsUpstream,
   includeIntron = FALSE,
   minGeneLen = nbinsGene,
   maxGeneLen = Inf
)
```

binOverRegions 27

# Arguments

### Author(s)

Jianhong Ou

### See Also

binOverRegions, plotBinOverRegions

### **Examples**

binOverRegions

coverage of chromosome regions

### **Description**

calculate the coverage of 5'UTR, CDS and 3'UTR per transcript per bin.

28 binOverRegions

### Usage

```
binOverRegions(
   cvglists,
   TxDb,
   upstream.cutoff = 1000L,
   downstream.cutoff = upstream.cutoff,
   nbinsCDS = 100L,
   nbinsUTR = 20L,
   nbinsUpstream = 20L,
   nbinsDownstream = nbinsUpstream,
   includeIntron = FALSE,
   minCDSLen = nbinsCDS,
   minUTRLen = nbinsUTR,
   maxCDSLen = Inf,
   maxUTRLen = Inf
)
```

# **Arguments**

### Author(s)

Jianhong Ou

#### See Also

binOverGene, plotBinOverRegions

```
if(Sys.getenv("USER")=="jianhongou"){
path <- system.file("extdata", package="ChIPpeakAnno")
library(TxDb.Hsapiens.UCSC.hg19.knownGene)
library(rtracklayer)
files <- dir(path, "bigWig")
if(.Platform$OS.type != "windows"){
cvglists <- lapply(file.path(path, files), import,</pre>
```

```
format="BigWig", as="RleList")
names(cvglists) <- sub(".bigWig", "", files)
d <- binOverRegions(cvglists, TxDb.Hsapiens.UCSC.hg19.knownGene)
plotBinOverRegions(d)
}
}</pre>
```

ChIPpeakAnno-deprecated

Deprecated Functions in Package ChIPpeakAnno

# Description

These functions are provided for compatibility with older versions of R only, and may be defunct as soon as the next release.

### **Arguments**

Peaks1 GRanges: See example below.
Peaks2 GRanges: See example below.

maxgap, minoverlap

Used in the internal call to findOverlaps() to detect overlaps. See ?findOverlaps

in the **IRanges** package for a description of these arguments.

multiple TRUE or FALSE: TRUE may return multiple overlapping peaks in Peaks2 for

one peak in Peaks1; FALSE will return at most one overlapping peaks in Peaks2 for one peak in Peaks1. This parameter is kept for backward compatibility,

please use select.

NameOfPeaks1 Name of the Peaks1, used for generating column name.

NameOfPeaks2 Name of the Peaks2, used for generating column name.

select all may return multiple overlapping peaks, first will return the first overlapping

peak, last will return the last overlapping peak and arbitrary will return one of

the overlapping peaks.

annotate Include overlapFeature and shortestDistance in the OverlappingPeaks or not. 1

means yes and 0 means no. Default to 0.

ignore.strand When set to TRUE, the strand information is ignored in the overlap calculations.

connectedPeaks If multiple peaks involved in overlapping in several groups, set it to "merge"

will count it as only 1, while set it to "min" will count it as the minimal involved

peaks in any concered groups

... Objects of GRanges: See also find0verlaps0fPeaks.

### Details

findOverlappingPeaks is now deprecated wrappers for findOverlapsOfPeaks

# See Also

Deprecated, findOverlapsOfPeaks, toGRanges

cnt0verlaps

count overlaps

# Description

Count overlaps with max gap.

# Usage

```
cntOverlaps(A, B, maxgap = 0L, ...)
```

### **Arguments**

A, B A GRanges object. A = 0 A single integer >= 0.

... parameters passed to numOverlaps#'

condenseMatrixByColnames

Condense matrix by colnames

# Description

Condense matrix by colnames

# Usage

```
condenseMatrixByColnames(mx, iname, sep = ";", cnt = FALSE)
```

# **Arguments**

mx a matrix to be condensed

iname the name of the column to be condensed sep separator for condensed values, default;

cnt TRUE/FALSE specifying whether adding count column or not?

### Value

dataframe of condensed matrix

convert2EntrezID 31

### Author(s)

Jianhong Ou, Lihua Julie Zhu

### **Examples**

```
a<-matrix(c(rep(rep(1:5,2),2),rep(1:10,2)),ncol=4)
colnames(a)<-c("con.1","con.2","index.1","index.2")
condenseMatrixByColnames(a,"con.1")
condenseMatrixByColnames(a,2)</pre>
```

convert2EntrezID

Convert other common IDs to entrez gene ID.

### **Description**

Convert other common IDs such as ensemble gene id, gene symbol, refseq id to entrez gene ID leveraging organism annotation dataset. For example, org.Hs.eg.db is the dataset from orgs.Hs.eg.db package for human, while org.Mm.eg.db is the dataset from the org.Mm.eg.db package for mouse.

# Usage

```
convert2EntrezID(IDs, orgAnn, ID_type = "ensembl_gene_id")
```

# Arguments

IDs a vector of IDs such as ensembl gene ids

orgAnn organism annotation dataset such as org.Hs.eg.db

ID\_type type of ID: can be ensemble\_gene\_id, gene\_symbol or refseq\_id

# Value

vector of entrez ids

# Author(s)

Lihua Julie Zhu

```
ensemblIDs = c("ENSG00000115956", "ENSG00000071082", "ENSG00000071054",
  "ENSG000000115594", "ENSG00000115594", "ENSG00000115598", "ENSG00000170417")
library(org.Hs.eg.db)
entrezIDs = convert2EntrezID(IDs=ensemblIDs, orgAnn="org.Hs.eg.db",
  ID_type="ensembl_gene_id")
```

32 countPatternInSeqs

countPatternInSeqs

Output total number of patterns found in the input sequences

# Description

Output total number of patterns found in the input sequences

# Usage

```
countPatternInSeqs(pattern, sequences)
```

### **Arguments**

pattern DNAstringSet object sequences a vector of sequences

### Value

Total number of occurrence of the pattern in the sequences

# Author(s)

Lihua Julie Zhu

# See Also

summarizePatternInPeaks, translatePattern

cumulativePercentage 33

cumulativePercentage Plot the cumulative percentage tag allocation in sample

### **Description**

Plot the difference between the cumulative percentage tag allocation in paired samples.

### Usage

```
cumulativePercentage(bamfiles, gr, input = 1, binWidth = 1000, ...)
```

### **Arguments**

bamfiles Bam file names.

gr An object of GRanges

input Which file name is input. default 1.

binWidth The width of each bin.

... parameter for summarizeOverlaps.

### Value

A list of data.frame with the cumulative percentages.

# Author(s)

Jianhong Ou

#### References

Normalization, bias correction, and peak calling for ChIP-seq Aaron Diaz, Kiyoub Park, Daniel A. Lim, Jun S. Song Stat Appl Genet Mol Biol. Author manuscript; available in PMC 2012 May 3.Published in final edited form as: Stat Appl Genet Mol Biol. 2012 Mar 31; 11(3): 10.1515/1544-6115.1750/j/sagmb.2012.11.issue-3/1544-6115.1750/1544-6115.1750.xml. Published online 2012 Mar 31. doi: 10.1515/1544-6115.1750 PMCID: PMC3342857

```
## Not run:
path <- system.file("extdata", "reads", package="MMDiffBamSubset")
files <- dir(path, "bam$", full.names = TRUE)
library(BSgenome.Hsapiens.UCSC.hg19)
gr <- as(seqinfo(Hsapiens)["chr1"], "GRanges")
cumulativePercentage(files, gr)
## End(Not run)</pre>
```

34 downstreams

downstreams

Get downstream coordinates

# **Description**

Returns an object of the same type and length as x containing downstream ranges. The output range is defined as

# Usage

```
downstreams(gr, upstream, downstream)
```

# Arguments

```
gr A GenomicRanges object upstream, downstream non-negative interges.
```

# **Details**

```
(end(x) - upstream) to (end(x) + downstream - 1) for ranges on the + and * strand, and as (start(x) - downstream + 1) to (start(x) + downstream) for ranges on the - strand.
```

Note that the returned object might contain out-of-bound ranges.

# Value

A GenomicRanges object

```
gr <- GRanges("chr1", IRanges(rep(10, 3), width=6), c("+", "-", "*")) downstreams(gr, 2, 2)
```

egOrgMap 35

	<i>C</i> .	1 .	.1		c i	1			1
egOrgMap	Convert	between	the	пате	of t	ne	organism	annotation	раскаде
	("OrgDb	") and the	nan	ne of th	ne org	gani	ism.		

# Description

Give a species name and return the organism annotation package name or give an organism annotation package name then return the species name.

# Usage

```
egOrgMap(name)
```

### **Arguments**

name

The name of the organism annotation package or the species.

# Value

A object of character

# Author(s)

Jianhong Ou

# **Examples**

```
egOrgMap("org.Hs.eg.db")
egOrgMap("Mus musculus")
```

enrichedG0

Enriched Gene Ontology terms used as example

# Description

Enriched Gene Ontology terms used as example

# Usage

enrichedG0

36 enrichedGO

#### **Format**

A list of 3 dataframes.

```
list("bp") dataframe described the enriched biological process with 9 columns go.id:GO biological process id go.term:GO biological process term go.Definition:GO biological process description Ontology: Ontology branch, i.e. BP for biological process count.InDataset: count of this GO term in this dataset count.InGenome: count of this GO term in the genome pvalue: pvalue from the hypergeometric test
```

totaltermInDataset: count of all GO terms in this dataset totaltermInGenome: count of all GO terms in the genome

list("mf") dataframe described the enriched molecular function with the following 9 columns

go.id:GO molecular function id go.term:GO molecular function term go.Definition:GO molecular function description Ontology: Ontology branch, i.e. MF for molecular function count.InDataset: count of this GO term in this dataset count.InGenome: count of this GO term in the genome pvalue: pvalue from the hypergeometric test

totaltermInDataset: count of all GO terms in this dataset

totaltermInGenome: count of all GO terms in the genome

list("cc") dataframe described the enriched cellular component the following 9 columns

go.id:GO cellular component id go.term:GO cellular component term go.Definition:GO cellular component description Ontology: Ontology type, i.e. CC for cellular component count.InDataset: count of this GO term in this dataset count.InGenome: count of this GO term in the genome

pvalue: pvalue from the hypergeometric test

totaltermInDataset: count of all GO terms in this dataset totaltermInGenome: count of all GO terms in the genome

#### Author(s)

Lihua Julie Zhu

# **Examples**

data(enrichedGO)
dim(enrichedGO\$mf)
dim(enrichedGO\$cc)
dim(enrichedGO\$bp)

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enrichmentPlot

plot enrichment results

# Description

Plot the GO/KEGG/reactome enrichment results

### Usage

```
enrichmentPlot(
  res,
  n = 20,
  strlength = Inf,
  style = c("v", "h"),
  label_wrap = 40,
  label_substring_to_remove = NULL,
  orderBy = c("pvalue", "termId", "none")
)
```

### **Arguments**

res output of getEnrichedGO, getEnrichedPATH. number of terms to be plot. strlength shorten the description of term by the number of char. plot vertically or horizontally style soft wrap the labels (i.e. descriptions of the GO or PATHWAY terms), default to label\_wrap 40 characters. label\_substring\_to\_remove remove common substring from label, default to NULL. Special characters must be escaped. E.g. if you would like to remove "Homo sapiens (human)" from labels, you must use "Homo sapiens \\( human\\)". orderBy order the data by pvalue, termId or none.

#### Value

an object of ggplot

### Author(s)

Jianhong Ou, Kai Hu

38 estFragmentLength

#### **Examples**

```
data(enrichedGO)
enrichmentPlot(enrichedGO)
if (interactive()||Sys.getenv("USER")=="jianhongou") {
     library(org.Hs.eg.db)
     library(GO.db)
     bed <- system.file("extdata", "MACS_output.bed", package="ChIPpeakAnno")</pre>
     gr1 <- toGRanges(bed, format="BED", header=FALSE)</pre>
     gff <- system.file("extdata", "GFF_peaks.gff", package="ChIPpeakAnno")</pre>
     gr2 <- toGRanges(gff, format="GFF", header=FALSE, skip=3)</pre>
     library(EnsDb.Hsapiens.v75) ##(hg19)
     annoData <- toGRanges(EnsDb.Hsapiens.v75)</pre>
     gr1.anno <- annoPeaks(gr1, annoData)</pre>
     gr2.anno <- annoPeaks(gr2, annoData)</pre>
     over <- lapply(GRangesList(gr1=gr1.anno, gr2=gr2.anno),</pre>
                     getEnrichedGO, orgAnn="org.Hs.eg.db",
                     maxP=.05, minGOterm=10, condense=TRUE)
     enrichmentPlot(over$gr1)
     enrichmentPlot(over$gr2, style = "h")
 }
```

EnsDb2GR

EnsDb object to GRanges

# Description

convert EnsDb object to GRanges

#### **Usage**

```
EnsDb2GR(ranges, feature)
```

# **Arguments**

ranges an EnsDb object

feature feature type, could be disjointExons, gene, exon and transcript

estFragmentLength estimate the fragment length

### **Description**

estimate the fragment length for bam files

estFragmentLength 39

### Usage

```
estFragmentLength(
  bamfiles,
  index = bamfiles,
  plot = TRUE,
  lag.max = 1000,
  minFragmentSize = 100,
  ...
)
```

# Arguments

bamfiles The file names of the 'BAM' ('SAM' for asBam) files to be processed.

index The names of the index file of the 'BAM' file being processed; this is given without the '.bai' extension.

plot logical. If TRUE (the default) the acf is plotted.

lag.max maximum lag at which to calculate the acf. See acf

minFragmentSize

minimal fragment size to avoid the phantom peak.

... Not used.

### Value

numberic vector

#### Author(s)

Jianhong Ou

```
if(interactive() || Sys.getenv("USER")=="jianhongou"){
   path <- system.file("extdata", "reads", package="MMDiffBamSubset")
   if(file.exists(path)){
      WT.AB2 <- file.path(path, "WT_2.bam")
      Null.AB2 <- file.path(path, "Null_2.bam")
      Resc.AB2 <- file.path(path, "Resc_2.bam")
      estFragmentLength(c(WT.AB2, Null.AB2, Resc.AB2))
   }
}</pre>
```

40 estLibSize

estLibSize

estimate the library size

#### **Description**

estimate the library size of bam files

### Usage

```
estLibSize(bamfiles, index = bamfiles, ...)
```

# **Arguments**

bamfiles The file names of the 'BAM' ('SAM' for asBam) files to be processed.

index The names of the index file of the 'BAM' file being processed; this is given

without the '.bai' extension.

... Not used.

#### Value

numberic vector

### Author(s)

Jianhong Ou

```
if(interactive() || Sys.getenv("USER")=="jianhongou"){
   path <- system.file("extdata", "reads", package="MMDiffBamSubset")
   if(file.exists(path)){
      WT.AB2 <- file.path(path, "WT_2.bam")
      Null.AB2 <- file.path(path, "Null_2.bam")
      Resc.AB2 <- file.path(path, "Resc_2.bam")
      estLibSize(c(WT.AB2, Null.AB2, Resc.AB2))
   }
}</pre>
```

ExonPlusUtr.human.GRCh37

Gene model with exon, 5' UTR and 3' UTR information for human sapiens (GRCh37) obtained from biomaRt

# Description

Gene model with exon, 5' UTR and 3' UTR information for human sapiens (GRCh37) obtained from biomaRt

### Usage

ExonPlusUtr.human.GRCh37

#### **Format**

GRanges with slot start holding the start position of the exon, slot end holding the end position of the exon, slot rownames holding ensembl transcript id and slot space holding the chromosome location where the gene is located. In addition, the following variables are included.

```
list("strand") 1 for positive strand and -1 for negative strand
list("description") description of the transcript
list("ensembl_gene_id") gene id
list("utr5start") 5' UTR start
list("utr5end") 5' UTR end
list("utr3start") 3' UTR start
list("utr3end") 3' UTR end
```

### **Details**

used in the examples Annotation data obtained by: mart = useMart(biomart = "ensembl", dataset = "hsapiens\_gene\_ensembl") ExonPlusUtr.human.GRCh37 = getAnnotation(mart=human, feature-Type="ExonPlusUtr")

```
data(ExonPlusUtr.human.GRCh37)
slotNames(ExonPlusUtr.human.GRCh37)
```

featureAlignedDistribution

plot distribution in given ranges

# Description

plot distribution in the given feature ranges

# Usage

```
featureAlignedDistribution(
  cvglists,
  feature.gr,
  upstream,
  downstream,
  n.tile = 100,
  zeroAt,
  ...
)
```

#### **Arguments**

cvglists Output of featureAlignedSignal or a list of SimpleRleList or RleList

feature.gr An object of GRanges with identical width. If the width equal to 1, you can use

upstream and downstream to set the range for plot. If the width not equal to 1,

you can use zeroAt to set the zero point of the heatmap.

upstream, downstream

upstream or dwonstream from the feature.gr.

n.tile The number of tiles to generate for each element of feature.gr, default is 100

zeroAt zero point position of feature.gr

... any paramters could be used by matplot

#### Value

invisible matrix of the plot.

#### Author(s)

Jianhong Ou

#### See Also

See Also as featureAlignedSignal, featureAlignedHeatmap

#### **Examples**

featureAlignedExtendSignal

extract signals in given ranges from bam files

### Description

extract signals in the given feature ranges from bam files (DNAseq only). The reads will be extended to estimated fragement length.

### Usage

```
featureAlignedExtendSignal(
  bamfiles,
  index = bamfiles,
  feature.gr,
  upstream,
  downstream,
  n.tile = 100,
  fragmentLength,
  librarySize,
  pe = c("auto", "PE", "SE"),
  adjustFragmentLength,
  gal,
  ...
)
```

#### **Arguments**

bamfiles The file names of the 'BAM' ('SAM' for asBam) files to be processed.

index The names of the index file of the 'BAM' file being processed; this is given

without the '.bai' extension.

feature.gr An object of GRanges with identical width.

upstream, downstream

upstream or dwonstream from the feature.gr.

n. tile The number of tiles to generate for each element of feature.gr, default is 100

fragmentLength Estimated fragment length.

#### Value

A list of matrix. In each matrix, each row record the signals for corresponding feature.

#### Author(s)

Jianhong Ou

#### See Also

See Also as featureAlignedSignal, estLibSize, estFragmentLength

```
if(interactive() || Sys.getenv("USER")=="jianhongou"){
   path <- system.file("extdata", package="MMDiffBamSubset")</pre>
   if(file.exists(path)){
       WT.AB2 <- file.path(path, "reads", "WT_2.bam")</pre>
       Null.AB2 <- file.path(path, "reads", "Null_2.bam")</pre>
       Resc.AB2 <- file.path(path, "reads", "Resc_2.bam")</pre>
       peaks <- file.path(path, "peaks", "WT_2_Macs_peaks.xls")</pre>
       estLibSize(c(WT.AB2, Null.AB2, Resc.AB2))
       feature.gr <- toGRanges(peaks, format="MACS")</pre>
       feature.gr <- feature.gr[seqnames(feature.gr)=="chr1" &</pre>
                              start(feature.gr)>3000000 &
                              end(feature.gr)<75000000]
       sig <- featureAlignedExtendSignal(c(WT.AB2, Null.AB2, Resc.AB2),</pre>
                                feature.gr=reCenterPeaks(feature.gr, width=1),
                                upstream = 505,
                                downstream = 505,
                                n.tile=101,
                                fragmentLength=250,
                                librarySize=1e9)
       featureAlignedHeatmap(sig, reCenterPeaks(feature.gr, width=1010),
                          zeroAt=.5, n.tile=101)
}
```

featureAlignedHeatmap Heatmap representing signals in given ranges

### Description

plot heatmap in the given feature ranges

# Usage

```
featureAlignedHeatmap(
  cvglists,
  feature.gr,
  upstream,
  downstream,
  zeroAt,
  n.tile = 100,
  annoMcols = c(),
  sortBy = names(cvglists)[1],
  color = colorRampPalette(c("yellow", "red"))(50),
  lower.extreme,
  upper.extreme,
 margin = c(0.1, 0.01, 0.15, 0.1),
 gap = 0.01,
 newpage = TRUE,
 gp = gpar(fontsize = 10),
)
```

### **Arguments**

cvglists	Output of	eature Aligne	edSignal or a	list of Sim	oleRleList or RleList

feature.gr An object of GRanges with identical width. If the width equal to 1, you can use

upstream and downstream to set the range for plot. If the width not equal to 1,

you can use zeroAt to set the zero point of the heatmap.

upstream, downstream

upstream or dwonstream from the feature.gr. It must keep same as feature-

AlignedSignal. It is used for x-axis label.

zeroAt zero point position of feature.gr

n.tile The number of tiles to generate for each element of feature.gr, default is 100

annoMcols The columns of metadata of feature.gr that specifies the annotations shown of

the right side of the heatmap.

sortBy Sort the feature.gr by columns by annoMcols and then the signals of the given

samples. Default is the first sample. Set to NULL to disable sort.

color vector of colors used in heatmap

featureAlignedSignal

lower.extreme, upper.extreme

The lower and upper boundary value of each samples

margin Margin for of the plot region.

gap Gap between each heatmap columns.

newpage Call grid.newpage or not. Default, TRUE

gp A gpar object can be used for text.

... Not used.

#### Value

invisible gList object.

### Author(s)

Jianhong Ou

#### See Also

See Also as featureAlignedSignal, featureAlignedDistribution

# **Examples**

featureAlignedSignal extract signals in given ranges

### **Description**

extract signals in the given feature ranges

### Usage

```
featureAlignedSignal(
  cvglists,
  feature.gr,
  upstream,
  downstream,
  n.tile = 100,
   ...
)
```

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# **Arguments**

cvglists List of SimpleRleList or RleList

feature.gr An object of GRanges with identical width.

upstream, downstream

Set the feature.gr to upstream and dwonstream from the center of the feature.gr if they are set.

n.tile The number of tiles to generate for each element of feature.gr, default is 100

A list of matrix. In each matrix, each row record the signals for corresponding feature. rownames of the matrix show the seqnames and coordinates.

### Author(s)

Value

Jianhong Ou

### See Also

See Also as featureAlignedHeatmap, featureAlignedDistribution

Not used.

### **Examples**

findEnhancers

Find possible enhancers depend on DNA interaction data

### **Description**

Find possible enhancers by data from chromosome conformation capture techniques such as 3C, 5C or HiC.

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#### Usage

```
findEnhancers(
  peaks,
  annoData,
  DNAinteractiveData,
  bindingType = c("nearestBiDirectionalPromoters", "startSite", "endSite"),
  bindingRegion = c(-5000, 5000),
  ignore.peak.strand = TRUE,
  ...
)
```

#### **Arguments**

peaks peak list, GRanges object
annoData annotation data, GRanges object

DNAinteractiveData

DNA interaction data, GRanges object with interaction blocks informations, GInteractions object, or BEDPE file which could be imported by importGInteractions or BiocIO::import or assembly in following list: hg38, hg19, mm10, danRer10, danRer11.

bindingType

Specifying the criteria to associate peaks with annotation. Here is how to use it together with the parameter bindingRegion. The annotation will be shift to a new position depend on the DNA interaction region.

- To obtain peaks within 5kb upstream and up to 3kb downstream of shift TSS within the gene body, set bindingType = "startSite" and bindingRegion = c(-5000, 3000)
- To obtain peaks up to 5kb upstream within the gene body and 3kb down-stream of shift gene/Exon End, set bindingType = "endSite" and bindingRegion = c(-5000, 3000)
- To obtain peaks with nearest bi-directional enhancer regions within 5kb upstream and 3kb downstream of shift TSS, set bindingType = "nearest-BiDirectionalPromoters" and bindingRegion = c(-5000, 3000)

**startSite** start position of the feature (strand is considered) **endSite** end position of the feature (strand is considered)

**nearestBiDirectionalPromoters** nearest enhancer regions from both direction of the peaks (strand is considered). It will report bidirectional enhancer regions if there are enhancer regions in both directions in the given region (defined by bindingRegion). Otherwise, it will report the closest enhancer regions in one direction.

bindingRegion

Annotation range used together with bindingType, which is a vector with two integer values, default to c (-5000, 5000). The first one must be no bigger than 0. And the sec ond one must be no less than 1. For details, see bindingType.

ignore.peak.strand

ignore the peaks strand or not.

.. Not used.

### Value

Output is a GRanges object of the annotated peaks.

#### Author(s)

Jianhong Ou

#### See Also

See Also as annotatePeakInBatch

### **Examples**

findMotifsInPromoterSeqs

Find occurence of input motifs in the promoter regions of the input gene list

### **Description**

Find occurence of input motifs in the promoter regions of the input gene list

### Usage

```
findMotifsInPromoterSeqs(
  patternFilePath1,
  patternFilePath2,
  findPairedMotif = FALSE,
  BSgenomeName,
  txdb,
  geneIDs,
  upstream = 5000L,
  downstream = 5000L,
  name.motif1 = "motif1",
  name.motif2 = "motif2",
  max.distance = 100L,
  min.distance = 1L,
  motif.orientation = c("both", "motif1UpstreamOfMotif2", "motif2UpstreamOfMoif1"),
```

```
ignore.strand = FALSE,
format = "fasta",
skip = 0L,
motif1LocForDistance = "end",
motif2LocForDistance = "start",
outfile,
append = FALSE
)
```

#### **Arguments**

patternFilePath1

File path containing a list of known motifs. Required

patternFilePath2

File path containing a motif required to be in the flanking regions of the motif(s) in the first file, i.e, patternFilePath1. Required if findPairedMotif is set to TRUE

findPairedMotif

Find motifs in paired configuration only or not. Default FALSE

BSgenomeName A BSgenome object. For a list of existing Bsgenomes, please refer use the func-

tion available.genomes in BSgenome package. For example,BSgenome.Hsapiens.UCSC.hg38 is for hg38, BSgenome.Hsapiens.UCSC.hg19 is for hg19, BSgenome.Mmusculus.UCSC.mm10 is for mm10, BSgenome.Celegans.UCSC.ce6 is for ce6 BSgenome.Rnorvegicus.UCSC.rn5

is for rn5, BSgenome.Drerio.UCSC.danRer7 is for Zv9, and BSgenome.Dmelanogaster.UCSC.dm3

is for dm3. Required

txdb A TxDb object. For creating and using TxDb object, please refer to GenomicFea-

tures package. For a list of existing TxDb object, please search for annotation

package starting with Txdb at http://www.bioconductor.org/packages/release/BiocViews.html#\_\_\_Annotasuch as TxDb.Rnorvegicus.UCSC.rn5.refGene for rat, TxDb.Mmusculus.UCSC.mm10.knownGene for mouse, TxDb.Hsapiens.UCSC.hg19.knownGene and TxDb.Hsapiens.UCSC.hg38.knownGene for human, TxDb.Dmelanogaster.UCSC.dm3.ensGene for Drosophila and TxDb.Celegans.UCSC.ce6.ens

for C.elegans

geneIDs One or more gene entrez IDs. For example the entrez ID for EWSIR is 2130

https://www.genecards.org/cgi-bin/carddisp.pl?gene=EWSR1 You can use the addGeneIDs function in ChIPpeakAnno to convert other types of Gene IDs to

entrez ID

upstream Number of bases upstream of the TSS to search for the motifs. Default 5000L

downstream Number of bases downstream of the TSS to search for the motifs. Default 5000L

name.motif1 Name of the motif in inputfilePath2 for labeling the output file column. Default

motif1. used only when searching for motifs in paired configuration

name.motif2 Name of the motif in inputfilePath2 for labeling the output file column. Default

motif2 used only when searching for motifs in paired configuration

max.distance maximum required gap between a paired motifs to be included in the output file.

Default 100L

min. distance Minimum required gap between a paired motifs to be included in the output file.

Default 1L

motif.orientation

Required relative oriention between paired motifs: both means any orientation, motif1UpstreamOfMotif2 means motif1 needs to be located on the upstream of motif2, and motif2UpstreamOfMoif1 means motif2 needs to be located on the

upstream of motif1. Default both

Specify whether paired motifs should be located on the same strand. Default ignore.strand

**FALSE** 

format The format of the files specified in inputFilePath1 and inputFilePath2. Default

skip Specify number of lines to skip at the beginning of the input file. Default 0L

motif1LocForDistance

Specify whether to use the start or end of the motif1 location to calculate distance between paired motifs. Only applicable when findPairedMotif is set to

TRUE. Default end

motif2LocForDistance

Specify whether to use the start or end of the motif2 location to calculate distance between paired motifs. Only applicable when findPairedMotif is set to

TRUE. Default start

outfile File path to save the search results

append Specify whether to append the results to the specified output file, i.e., outfile.

Default FALSE

#### **Details**

This function outputs the motif occuring locations in the promoter regions of input gene list and input motifs. It also can find paired motifs within specificed gap threshold

# Value

A vector of numeric. It is the background corrected log2-transformed ratios, CPMRatios or Odd-Ratios.

An object of GRanges with metadata "tx\_start", "tx\_end tx\_strand", "tx\_id", "tx\_name", "Gene ID", and motif specific information such as motif name, motif found, motif strand etc.

#### Author(s)

Lihua Julie Zhu, Kai Hu

```
library("BSgenome.Hsapiens.UCSC.hg38")
library("TxDb.Hsapiens.UCSC.hg38.knownGene")
patternFilePath1 =system.file("extdata", "motifIRF4.fa", package="ChIPpeakAnno")
patternFilePath2 =system.file("extdata", "motifAP1.fa", package="ChIPpeakAnno")
pairedMotifs <- findMotifsInPromoterSeqs(patternFilePath1 = patternFilePath1,</pre>
  patternFilePath2 = patternFilePath2,
```

```
findPairedMotif = TRUE,
  name.motif1 = "IRF4", name.motif2 = "AP1",
  BSgenomeName = BSgenome.Hsapiens.UCSC.hg38,
  geneIDs = 7486, txdb = TxDb.Hsapiens.UCSC.hg38.knownGene,
  outfile = "testPaired.xls")

unPairedMotifs <- findMotifsInPromoterSeqs(patternFilePath1 = patternFilePath1,
  BSgenomeName = BSgenome.Hsapiens.UCSC.hg38,
  geneIDs = 7486, txdb = TxDb.Hsapiens.UCSC.hg38.knownGene,
  outfile = "testUnPaired.xls")</pre>
```

findOverlappingPeaks Find the overlapping peaks for two peak ranges.

### **Description**

Find the overlapping peaks for two input peak ranges.

### Usage

```
findOverlappingPeaks(
   Peaks1,
   Peaks2,
   maxgap = -1L,
   minoverlap = 0L,
   multiple = c(TRUE, FALSE),
   NameOfPeaks1 = "TF1",
   NameOfPeaks2 = "TF2",
   select = c("all", "first", "last", "arbitrary"),
   annotate = 0,
   ignore.strand = TRUE,
   connectedPeaks = c("min", "merge"),
   ...
)
```

### **Arguments**

Peaks1 GRanges: See example below.
Peaks2 GRanges: See example below.

maxgap, minoverlap

Used in the internal call to findOverlaps() to detect overlaps. See ?findOverlaps in the **IRanges** package for a description of these arguments.

multiple

TRUE or FALSE: TRUE may return multiple overlapping peaks in Peaks2 for one peak in Peaks1; FALSE will return at most one overlapping peaks in Peaks2 for one peak in Peaks1. This parameter is kept for backward compatibility, please use select.

NameOfPeaks1 Name of the Peaks1, used for generating column name. NameOfPeaks2 Name of the Peaks2, used for generating column name.

select all may return multiple overlapping peaks, first will return the first overlapping

peak, last will return the last overlapping peak and arbitrary will return one of

the overlapping peaks.

Include overlapFeature and shortestDistance in the OverlappingPeaks or not. 1 annotate

means yes and 0 means no. Default to 0.

When set to TRUE, the strand information is ignored in the overlap calculations. ignore.strand

If multiple peaks involved in overlapping in several groups, set it to "merge" connectedPeaks

will count it as only 1, while set it to "min" will count it as the minimal involved

peaks in any concered groups

Objects of GRanges: See also findOverlapsOfPeaks.

#### **Details**

The new function findOverlapsOfPeaks is recommended.

Efficiently perform overlap queries with an interval tree implemented in IRanges.

#### Value

OverlappingPeaks

a data frame consists of input peaks information with added information: overlapFeature (upstream: peak1 resides upstream of the peak2; downstream: peak1 resides downstream of the peak2; inside: peak1 resides inside the peak2 entirely; overlapStart: peak1 overlaps with the start of the peak2; overlapEnd: peak1 overlaps with the end of the peak2; includeFeature: peak1 include the peak2 entirely) and shortestDistance (shortest distance between the overlapping peaks)

MergedPeaks GRanges contains merged overlapping peaks

### Author(s)

Lihua Julie Zhu

#### References

1.Interval tree algorithm from: Cormen, Thomas H.; Leiserson, Charles E.; Rivest, Ronald L.; Stein, Clifford. Introduction to Algorithms, second edition, MIT Press and McGraw-Hill. ISBN 0-262-53196-8

2.Zhu L.J. et al. (2010) ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIPchip data. BMC Bioinformatics 2010, 11:237 doi:10.1186/1471-2105-11-237

3. Zhu L (2013). Integrative analysis of ChIP-chip and ChIP-seq dataset. In Lee T and Luk ACS (eds.), Tilling Arrays, volume 1067, chapter 4, pp. -19. Humana Press. http://dx.doi.org/10.1007/978-1-62703-607-8\_8

### See Also

findOverlapsOfPeaks, annotatePeakInBatch, makeVennDiagram

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### **Examples**

```
if (interactive())
{
peaks1 =
    GRanges(segnames=c(6,6,6,6,5),
            IRanges(start=c(1543200,1557200,1563000,1569800,167889600),
                    end=c(1555199,1560599,1565199,1573799,167893599),
                    names=c("p1","p2","p3","p4","p5")),
            strand=as.integer(1))
peaks2 =
    GRanges(segnames=c(6,6,6,6,5),
            IRanges(start=c(1549800,1554400,1565000,1569400,167888600),
                    end=c(1550599,1560799,1565399,1571199,167888999),
                    names=c("f1","f2","f3","f4","f5")),
            strand=as.integer(1))
t1 =findOverlappingPeaks(peaks1, peaks2, maxgap=1000,
      NameOfPeaks1="TF1", NameOfPeaks2="TF2", select="all", annotate=1)
r = t1$OverlappingPeaks
pie(table(r$overlapFeature))
as.data.frame(t1$MergedPeaks)
```

findOverlapsOfPeaks

Find the overlapped peaks among two or more set of peaks.

### **Description**

Find the overlapping peaks for two or more (less than five) set of peak ranges.

# Usage

```
findOverlapsOfPeaks(
    ...,
    maxgap = -1L,
    minoverlap = 0L,
    ignore.strand = TRUE,
    connectedPeaks = c("keepAll", "min", "merge")
)
```

### **Arguments**

```
... Objects of GRanges: See example below. maxgap, minoverlap
```

Used in the internal call to findOverlaps() to detect overlaps. See ?findOverlaps in the **IRanges** package for a description of these arguments. If 0 < minoverlap < 1, the function will find overlaps by percentage covered of interval and the filter condition will be set to max covered percentage of overlapping peaks.

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ignore.strand

When set to TRUE, the strand information is ignored in the overlap calculations.

connectedPeaks

If multiple peaks are involved in any group of connected/overlapping peaks in any input peak list, set it to "merge" will add 1 to the overlapping counts, while set it to "min" will add the minimal involved peaks in each group of connected/overlapped peaks to the overlapping counts. Set it to "keepAll" will add the number of involved peaks for each peak list to the corresponding overlapping counts. In addition, it will output counts as if connectedPeaks were set to "min". For examples (https://support.bioconductor.org/p/133486/#133603), if 5 peaks in group1 overlap with 2 peaks in group 2, setting connectedPeaks to "merge" will add 1 to the overlapping counts; setting it to "keepAll" will add 5 peaks to count.group1, 2 to count.group2, and 2 to counts; setting it to "min" will add 2 to the overlapping counts.

#### **Details**

Efficiently perform overlap queries with an interval tree implemented with GRanges.

#### Value

return value is An object of overlappingPeaks.

venn\_cnt an object of VennCounts

peaklist a list consists of all overlapping peaks or unique peaks uniquePeaks an object of GRanges consists of all unique peaks

mergedPeaks an object of GRanges consists of all merged overlapping peaks

peaksInMergedPeaks

an object of GRanges consists of all peaks in each samples involved in the over-

lapping peaks

overlappingPeaks

a list of data frame consists of the annotation of all the overlapped peaks

all.peaks a list of GRanges object which contain the input peaks with formated rownames.

#### Author(s)

Jianhong Ou

#### References

1.Interval tree algorithm from: Cormen, Thomas H.; Leiserson, Charles E.; Rivest, Ronald L.; Stein, Clifford. Introduction to Algorithms, second edition, MIT Press and McGraw-Hill. ISBN 0-262-53196-8

2.Zhu L.J. et al. (2010) ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIP-chip data. BMC Bioinformatics 2010, 11:237doi:10.1186/1471-2105-11-237

3. Zhu L (2013). "Integrative analysis of ChIP-chip and ChIP-seq dataset." In Lee T and Luk ACS (eds.), Tilling Arrays, volume 1067, chapter 4, pp. -19. Humana Press. http://dx.doi.org/10.1007/978-1-62703-607-8\_8, http://link.springer.com/protocol/10.1007%2F978-1-62703-607-8\_8

#### See Also

annotatePeakInBatch, makeVennDiagram, getVennCounts, findOverlappingPeaks

### **Examples**

```
peaks1 <- GRanges(seqnames=c(6,6,6,6,5),
                 IRanges(start=c(1543200,1557200,1563000,1569800,167889600),
                         end=c(1555199,1560599,1565199,1573799,167893599),
                         names=c("p1","p2","p3","p4","p5")),
                 strand="+")
peaks2 <- GRanges(seqnames=c(6,6,6,6,5),
                  IRanges(start=c(1549800,1554400,1565000,1569400,167888600),
                          end=c(1550599,1560799,1565399,1571199,167888999),
                          names=c("f1","f2","f3","f4","f5")),
                  strand="+")
t1 <- findOverlapsOfPeaks(peaks1, peaks2, maxgap=1000)
makeVennDiagram(t1)
t1$venn_cnt
t1$peaklist
t2 <- findOverlapsOfPeaks(peaks1, peaks2, minoverlap = .5)</pre>
makeVennDiagram(t2)
t3 <- findOverlapsOfPeaks(peaks1, peaks2, minoverlap = .90)
makeVennDiagram(t3)
```

genomicElementDistribution

Genomic Element distribution

#### **Description**

Plot pie chart for genomic element distribution

#### Usage

```
genomicElementDistribution(
  peaks,
  TxDb,
  seqlev,
  nucleotideLevel = FALSE,
  ignore.strand = TRUE,
  promoterRegion = c(upstream = 2000, downstream = 100),
  geneDownstream = c(upstream = 0, downstream = 1000),
  labels = list(geneLevel = c(promoter = "Promoter", geneDownstream = "Downstream",
    geneBody = "Gene body", distalIntergenic = "Distal Intergenic"), ExonIntron = c(exon
    = "Exon", intron = "Intron", intergenic = "Intergenic"), Exons = c(utr5 = "5' UTR",
    utr3 = "3' UTR", CDS = "CDS", otherExon = "Other exon"), group = c(geneLevel =
```

```
"Transcript Level", promoterLevel = "Promoter Level", Exons = "Exon level",
    ExonIntron = "Exon/Intron/Intergenic")),
labelColors = c(promoter = "#E1F114", geneBody = "#9EFF00", geneDownstream = "#57CB1B",
    distalIntergenic = "#066A4B", exon = "#6600FF", intron = "#8F00FF", intergenic =
        "#DA00FF", utr5 = "#00FFDB", utr3 = "#00DFFF", CDS = "#00A0FF", otherExon =
        "#006FFF"),
    plot = TRUE,
    keepExonsInGenesOnly = TRUE,
    promoterLevel
)
```

#### Arguments

peaks peak list, GRanges object or a GRangesList.

TxDb an object of TxDb

sequence level should be involved. Default is all the sequence levels in intersect

of peaks and TxDb.

nucleotideLevel

Logical. Choose between peak centric and nucleotide centric view. Default=FALSE

ignore.strand logical. Whether the strand of the input ranges should be ignored or not. De-

fault=TRUE

promoterRegion numeric. The upstream and downstream of genes to define promoter region.

geneDownstream numeric. The upstream and downstream of genes to define gene downstream

region.

labels list. A list for labels for the genomic elements.

labelColors named character vector. The colors for each labels.

plot logic. Plot the pie chart for the genomic elements or not.

keepExonsInGenesOnly

logic. Keep the exons within annotated gene only.

promoterLevel list. The breaks, labels, and colors for divided range of promoters. The breaks

must be from  $5' \rightarrow 3'$  and the percentage will use the fixed precedence  $3' \rightarrow 5'$ 

#### **Details**

The distribution will be calculated by geneLevel, ExonIntron, and Exons The geneLevel will be categorized as promoter region, gene body, gene downstream and distal intergenic region. The ExonIntron will be categorized as exon, intron and intergenic. The Exons will be categorized as 5' UTR, 3'UTR and CDS. The precedence will follow the order of labels defination. For example, for ExonIntron, if a peak overlap with both exon and intron, and exon is specified before intron, then only exon will be incremented for the same example.

#### Value

Invisible list of data for plot.

### **Examples**

```
if (interactive() || Sys.getenv("USER")=="jianhongou"){
 data(myPeakList)
 if(require(TxDb.Hsapiens.UCSC.hg19.knownGene)){
 seqinfo(myPeakList) <-</pre>
  seqinfo(TxDb.Hsapiens.UCSC.hg19.knownGene)[seqlevels(myPeakList)]
 myPeakList <- GenomicRanges::trim(myPeakList)</pre>
 myPeakList <- myPeakList[width(myPeakList)>0]
   genomicElementDistribution(myPeakList,
        TxDb.Hsapiens.UCSC.hg19.knownGene)
    genomicElementDistribution(myPeakList,
        TxDb.Hsapiens.UCSC.hg19.knownGene,
        nucleotideLevel = TRUE)
   genomicElementDistribution(myPeakList,
        TxDb.Hsapiens.UCSC.hg19.knownGene,
        promoterLevel=list(
        #from 5' -> 3', fixed precedence 3' -> 5'
        breaks = c(-2000, -1000, -500, 0, 100),
        labels = c("upstream 1-2Kb", "upstream 0.5-1Kb",
                   "upstream <500b", "TSS - 100b"),
        colors = c("#FFE5CC", "#FFCA99",
                   "#FFAD65", "#FF8E32")))
 }
}
```

genomicElementUpSetR Genomic Element data for upset plot

#### Description

Prepare data for upset plot for genomic element distribution

#### Usage

```
genomicElementUpSetR(
   peaks,
   TxDb,
   seqlev,
   ignore.strand = TRUE,
   breaks = list(distal_upstream = c(-1e+05, -10000, -1, 1), proximal_upstream = c(-10000,
        -5000, -1, 1), distal_promoter = c(-5000, -2000, -1, 1), proximal_promoter = c(-2000,
        200, -1, 0), `5'UTR` = fiveUTRsByTranscript, `3'UTR` = threeUTRsByTranscript, CDS =
        cds, exon = exons, intron = intronsByTranscript, gene_body = genes,
   immediate_downstream = c(0, 2000, 1, 1), proximal_downstream = c(2000, 5000, 1, 1),
        distal_downstream = c(5000, 1e+05, 1, 1))
)
```

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### Arguments

peaks peak list, GRanges object or a GRangesList.

TxDb an object of TxDb

sequence level should be involved. Default is all the sequence levels in intersect

of peaks and TxDb.

ignore.strand logical. Whether the strand of the input ranges should be ignored or not. De-

fault=TRUE

breaks list. A list for labels and sets for the genomic elements. The element could be an

S4 method for signature 'TxDb' or a numeric vector with length of 4. The three numbers are c(upstream point, downstream point, promoter (-1) or downstream

(1), remove gene body or not (1: remove, 0: keep)).

#### **Details**

The data will be calculated by for each breaks. No precedence will be considered.

#### Value

list of data for plot.

#### **Examples**

```
if (interactive() || Sys.getenv("USER")=="jianhongou"){
  data(myPeakList)
  if(require(TxDb.Hsapiens.UCSC.hg19.knownGene)){
  seqinfo(myPeakList) <-
    seqinfo(TxDb.Hsapiens.UCSC.hg19.knownGene)[seqlevels(myPeakList)]
  myPeakList <- GenomicRanges::trim(myPeakList)
  myPeakList <- myPeakList[width(myPeakList)>0]
  x <- genomicElementUpSetR(myPeakList,
    TxDb.Hsapiens.UCSC.hg19.knownGene)
  library(UpSetR)
  upset(x$plotData, nsets=13, nintersects=NA)
  }
}</pre>
```

getAllPeakSequence

Obtain genomic sequences around the peaks

### **Description**

Obtain genomic sequences around the peaks leveraging the BSgenome and biomaRt package

### Usage

```
getAllPeakSequence(
  myPeakList,
  upstream = 200L,
  downstream = upstream,
  genome,
  AnnotationData
)
```

### **Arguments**

myPeakList An object of GRanges: See example below upstream upstream offset from the peak start, e.g., 200 downstream offset from the peak end, e.g., 200

genome BSgenome object or mart object. Please refer to available genomes in BSgenome

package and useMart in bioMaRt package for details

AnnotationData GRanges object with annotation information.

#### Value

GRanges with slot start holding the start position of the peak, slot end holding the end position of the peak, slot rownames holding the id of the peak and slot sequames holding the chromosome where the peak is located. In addition, the following variables are included:

upstream upstream offset from the peak start downstream offset from the peak end

sequence the sequence obtained

#### Author(s)

Lihua Julie Zhu, Jianhong Ou

### References

Durinck S. et al. (2005) BioMart and Bioconductor: a powerful link between biological biomarts and microarray data analysis. Bioinformatics, 21, 3439-3440.

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getAnnotation

Obtain the TSS, exon or miRNA annotation for the specified species

### **Description**

Obtain the TSS, exon or miRNA annotation for the specified species using the biomaRt package

### Usage

```
getAnnotation(
  mart,
  featureType = c("TSS", "miRNA", "Exon", "5utr", "3utr", "ExonPlusUtr", "transcript")
)
```

### **Arguments**

mart A mart object, see useMart of biomaRt package for details.

featureType TSS, miRNA, Exon, 5'UTR, 3'UTR, transcript or Exon plus UTR. The default

is TSS.

#### Value

GRanges with slot start holding the start position of the feature, slot end holding the end position of the feature, slot names holding the id of the feature, slot space holding the chromosome location where the feature is located. In addition, the following variables are included.

list("strand") 1 for positive strand and -1 for negative strand where the feature is located list("description")

description of the feeature such as gene

### Note

For featureType of TSS, start is the transcription start site if strand is 1 (plus strand), otherwise, end is the transcription start site.

Note that the version of the annotation db must match with the genome used for mapping because the coordinates may differ for different genome releases. For example, if you are using Mus\_musculus.v103 for mapping, you'd best also use EnsDb.Mmusculus.v103 for annotation. See Examples for more info.

#### Author(s)

Lihua Julie Zhu, Jianhong Ou, Kai Hu

### References

Durinck S. et al. (2005) BioMart and Bioconductor: a powerful link between biological biomarts and microarray data analysis. Bioinformatics, 21, 3439-3440.

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#### **Examples**

```
if (interactive() || Sys.getenv("USER")=="jianhongou" )
 library(biomaRt)
 mart <- useMart(biomart="ensembl", dataset="hsapiens_gene_ensembl")</pre>
 Annotation <- getAnnotation(mart, featureType="TSS")</pre>
}
# Below are 3 options to fetch the annotation file.
if (interactive() || Sys.getenv("USER")=="jianhongou" ){
## Option1: with the AnnotationHub package
library(AnnotationHub)
ah <- AnnotationHub()</pre>
EnsDb.Mmusculus <- query(ah, pattern = c("Mus musculus", "EnsDb"))</pre>
EnsDb.Mmusculus.v101 <- EnsDb.Mmusculus[[length(EnsDb.Mmusculus)]]</pre>
class(EnsDb.Mmusculus.v101)
## Option2: with the getAnnotation() function
library(ChIPpeakAnno)
library(biomaRt)
listMarts()
mart <- useMart(biomart="ENSEMBL_MART_ENSEMBL",</pre>
               dataset="mmusculus_gene_ensembl")
Annotation <- getAnnotation(mart)</pre>
# Note that getAnnotation() queries biomart, which is always up-to-date.
## Option3: build your own EnsDb package
## This may need extra effort, and the ?makeEnsembldbPackage
## is a good starting point.
}
```

getEnrichedG0

Obtain enriched gene ontology (GO) terms that near the peaks

#### **Description**

Obtain enriched gene ontology (GO) terms based on the features near the enriched peaks using GO.db package and GO gene mapping package such as org.Hs.db.eg to obtain the GO annotation and using hypergeometric test (phyper) and multtest package for adjusting p-values

# Usage

```
getEnrichedGO(
   annotatedPeak,
   orgAnn,
   feature_id_type = "ensembl_gene_id",
   maxP = 0.01,
```

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```
minGOterm = 10,
multiAdjMethod = NULL,
condense = FALSE,
removeAncestorByPval = NULL,
keepByLevel = NULL,
subGroupComparison = NULL)
```

#### **Arguments**

annotatedPeak A GRanges object or a vector of feature IDs

orgAnn Organism annotation package such as org.Hs.eg.db for human and org.Mm.eg.db

for mouse, org.Dm.eg.db for fly, org.Rn.eg.db for rat, org.Sc.eg.db for yeast and

org.Dr.eg.db for zebrafish

feature\_id\_type

The feature type in annotatedPeak such as ensembl\_gene\_id, refseq\_id, gene\_symbol

or entrez\_id

maxP The maximum p-value to be considered to be significant

minGOterm The minimum count in a genome for a GO term to be included

multiAdjMethod The multiple testing procedures, for details, see mt.rawp2adjp in multtest pack-

age

condense Condense the results or not.

removeAncestorByPval

Remove ancestor by p-value. P-value is calculated by fisher exact test. If gene number in all of the children is significant greater than it in parent term, the

parent term will be removed from the list.

keepByLevel If the shortest path from the go term to 'all' is greater than the given level, the

term will be removed.

subGroupComparison

A logical vector to split the peaks into two groups. The enrichment analysis will compare the over-present GO terms in TRUE group and FALSE group separately. The analysis will split into two steps: 1. enrichment analysis for TRUE group by hypergeometric test; 2. enrichment analysis for TRUE over FALSE group by Fisher's Exact test for the enriched GO terms. To keep the output same format, if you want to compare FALSE vs TRUE, please repeat the analysis by inverting the parameter. Default is NULL.

### Value

#### A list with 3 elements

list("bp")

enriched biological process with the following 9 variables
go.id:GO biological process id
go.term:GO biological process term
go.Definition:GO biological process description
Ontology: Ontology branch, i.e. BP for biological process

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count.InDataset: count of this GO term in this dataset count.InGenome: count of this GO term in the genome pvalue: pvalue from the hypergeometric test totaltermInDataset: count of all GO terms in this dataset totaltermInGenome: count of all GO terms in the genome enriched molecular function with the following 9 variables go.id:GO molecular function id go.term:GO molecular function term go.Definition:GO molecular function description Ontology: Ontology branch, i.e. MF for molecular function count.InDataset: count of this GO term in this dataset count.InGenome: count of this GO term in the genome pvalue: pvalue from the hypergeometric test totaltermInDataset: count of all GO terms in this dataset totaltermInGenome: count of all GO terms in the genome enriched cellular component the following 9 variables go.id:GO cellular component id go.term:GO cellular component term go.Definition:GO cellular component description Ontology: Ontology type, i.e. CC for cellular component count.InDataset: count of this GO term in this dataset count.InGenome: count of this GO term in the genome pvalue: pvalue from the hypergeometric test totaltermInDataset: count of all GO terms in this dataset

#### Author(s)

list("mf")

list("cc")

Lihua Julie Zhu. Jianhong Ou for subGroupComparison

### References

Johnson, N. L., Kotz, S., and Kemp, A. W. (1992) Univariate Discrete Distributions, Second Edition. New York: Wiley

totaltermInGenome: count of all GO terms in the genome

#### See Also

phyper, hyperGtest

```
data(enrichedGO)
enrichedGO$mf[1:10,]
enrichedGO$bp[1:10,]
enrichedGO$cc
if (interactive()) {
```

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getEnrichedPATH

Obtain enriched PATH that near the peaks

# **Description**

Obtain enriched PATH that are near the peaks using path package such as reactome.db and path mapping package such as org.Hs.db.eg to obtain the path annotation and using hypergeometric test (phyper) and multtest package for adjusting p-values

#### Usage

```
getEnrichedPATH(
  annotatedPeak,
  orgAnn,
  pathAnn,
  feature_id_type = "ensembl_gene_id",
  maxP = 0.01,
  minPATHterm = 10,
  multiAdjMethod = NULL,
  subGroupComparison = NULL
)
```

### **Arguments**

annotatedPeak GRanges such as data(annotatedPeak) or a vector of feature IDs

orgAnn organism annotation package such as org.Hs.eg.db for human and org.Mm.eg.db

for mouse, org.Dm.eg.db for fly, org.Rn.eg.db for rat, org.Sc.eg.db for yeast and

org.Dr.eg.db for zebrafish

pathAnn pathway annotation package such as KEGG.db (deprecated), reactome.db, KEG-

**GREST** 

feature\_id\_type

the feature type in annotatedPeakRanges such as ensembl\_gene\_id, refseq\_id,

gene\_symbol or entrez\_id

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maxP maximum p-value to be considered to be significant minPATHterm minimum count in a genome for a path to be included

multiAdjMethod multiple testing procedures, for details, see mt.rawp2adjp in multtest package subGroupComparison

A logical vector to split the peaks into two groups. The enrichment analysis will compare the over-present GO terms in TRUE group and FALSE group separately. The analysis will split into two steps: 1. enrichment analysis for TRUE group by hypergeometric test; 2. enrichment analysis for TRUE over FALSE group by Fisher's Exact test for the enriched GO terms. To keep the output same format, if you want to compare FALSE vs TRUE, please repeat the analysis by inverting the parameter. Default is NULL.

#### Value

A dataframe of enriched path with the following variables.

path.id KEGG PATH ID

EntrezID Entrez ID

count.InDataset

count of this PATH in this dataset

count.InGenome count of this PATH in the genome pvalue pvalue from the hypergeometric test

totaltermInDataset

count of all PATH in this dataset

totaltermInGenome

count of all PATH in the genome

PATH PATH name

#### Author(s)

Jianhong Ou, Kai Hu

#### References

Johnson, N. L., Kotz, S., and Kemp, A. W. (1992) Univariate Discrete Distributions, Second Edition. New York: Wiley

#### See Also

phyper, hyperGtest

```
if (interactive()||Sys.getenv("USER")=="jianhongou") {
  data(annotatedPeak)
  library(org.Hs.eg.db)
  library(reactome.db)
  enriched.PATH = getEnrichedPATH(annotatedPeak, orgAnn="org.Hs.eg.db",
```

getGeneSeq 67

getGeneSeq

Get gene sequence using the biomaRt package

# Description

Get gene sequence using the biomaRt package

### Usage

```
getGeneSeq(LocationParameters, mart)
```

# **Arguments**

LocationParameters

c(ensembl\_gene\_id, distance from the peak to the transcription start site of the gene with the above ensemblID, upstream offset from the peak, downstream

offset from the peak, Gene Start, Gene End)

mart see useMart of bioMaRt package for details

#### Value

a list with the following items

feature\_id ensemble gene ID

distancetoFeature

distance from the peak to the transcriptionstart site of the gene with the above

ensembl gene ID

upstream upstream offset from the peakStart downstream downstream offset from the peakEnd

seq sequence obtained around the peak with above upstream and downstream offset

#### Note

internal function not intended to be called directly by users

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#### Author(s)

Lihua Julie Zhu

### **Examples**

```
if (interactive())
mart <- useMart(biomart="ensembl", dataset="drerio_gene_ensembl")</pre>
LocationParameters =c("ENSDARG00000054562",400, 750, 750,40454140,40454935)
getGeneSeq(LocationParameters, mart)
LocationParameters =c("ENSDARG00000054562",752, 750, 750, 40454140, 40454935)
getGeneSeq(LocationParameters, mart)
LocationParameters =c("ENSDARG00000054562",750, 750, 750, 40454140,40454935)
getGeneSeq(LocationParameters, mart)
 LocationParameters =c("ENSDARG00000054562",-2, 750, 750, 40454140, 40454935)
 getGeneSeq(LocationParameters, mart)
 LocationParameters =c("ENSDARG00000054562",0, 750, 750, 40454140,40454935)
 getGeneSeq(LocationParameters, mart)
 LocationParameters =c("ENSDARG00000054562",2, 750, 750,40454140,40454935)
 getGeneSeq(LocationParameters, mart)
 LocationParameters =c("ENSDARG00000054562",1000, 750, 750, 40454140, 40454935)
 getGeneSeq(LocationParameters, mart)
}
```

getG0

Obtain gene ontology (GO) terms for given genes

#### **Description**

Obtain gene ontology (GO) terms useing GO gene mapping package such as org.Hs.db.eg to obtain the GO annotation.

#### Usage

```
getGO(all.genes, orgAnn = "org.Hs.eg.db", writeTo, ID_type = "gene_symbol")
```

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### **Arguments**

all.genes A character vector of feature IDs

orgAnn Organism annotation package such as org.Hs.eg.db for human and org.Mm.eg.db

for mouse, org.Dm.eg.db for fly, org.Rn.eg.db for rat, org.Sc.eg.db for yeast and

org.Dr.eg.db for zebrafish

writeTo File path for output table

ID\_type The feature type in annotatedPeak such as ensembl\_gene\_id, refseq\_id, gene\_symbol

#### Value

An invisible table with genes and GO terms.

### Author(s)

Lihua Julie Zhu

#### See Also

getEnrichedGO

# **Examples**

```
if (interactive()) {
   data(annotatedPeak)
   library(org.Hs.eg.db)
   getGO(annotatedPeak[1:6]$feature,
        orgAnn="org.Hs.eg.db",
        ID_type="ensembl_gene_id")
}
```

getUniqueGOidCount

get the count for each unique GO ID

# **Description**

get the count for each unique GO ID

# Usage

```
getUniqueGOidCount(goList)
```

# Arguments

goList

a set of GO terms as character vector

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#### Value

a list with 2 variables

GOterm a vector of GO terms as character vector

GOcount counts corresponding to the above GOterm as numeric vector

#### Note

internal function not intended to be called directly by users

### Author(s)

Lihua Julie Zhu

#### See Also

getEnrichedGO

#### **Examples**

getVennCounts

Obtain Venn Counts for Venn Diagram, internal function for makeVennDigram

### **Description**

Obtain Venn Counts for peak ranges using chromosome ranges or feature field, internal function for makeVennDigram

# Usage

```
getVennCounts(
    ...,
    maxgap = -1L,
    minoverlap = 0L,
    by = c("region", "feature", "base"),
    ignore.strand = TRUE,
    connectedPeaks = c("min", "merge", "keepAll")
)
```

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### Arguments

by

... Objects of GRanges. See example below.

maxgap, minoverlap

Used in the internal call to findOverlaps() to detect overlaps. See ?findOverlaps in the **IRanges** package for a description of these arguments.

in the **Tranges** package for a description of these arguments

region, feature or base, default region. feature means using feature field in the GRanges for calculating overlap, region means using chromosome range for calculating overlap, and have means using calculating expedient in purchasidal level.

culating overlap, and base means using calculating overlap in nucleotide level.

ignore.strand When set to TRUE, the strand information is ignored in the overlap calculations.

connectedPeaks If multiple peaks involved in overlapping in several groups, set it to "merge" will count it as only 1, while set it to "min" will count it as the minimal involved

peaks in any concered groups

#### Value

vennCounts

vennCounts objects containing counts for Venn Diagram generation, see details in limma package vennCounts

#### Author(s)

Jianhong Ou

#### See Also

makeVennDiagram, findOverlappingPeaks

```
if(interactive() || Sys.getenv("USER")=="jianhongou"){
peaks1 = GRanges(seqnames=c("1", "2", "3"),
                 IRanges(start = c(967654, 2010897, 2496704),
                            end = c(967754, 2010997, 2496804),
                            names = c("Site1", "Site2", "Site3")),
                   strand=as.integer(1),
                   feature=c("a","b", "c"))
 peaks2 =
      GRanges(seqnames= c("1", "2", "3", "1", "2"),
                    IRanges(start=c(967659, 2010898, 2496700, 3075866, 3123260),
                         end=c(967869, 2011108, 2496920, 3076166, 3123470),
                         names = c("t1", "t2", "t3", "t4", "t5")),
                    strand = c(1L, 1L, -1L, -1L, 1L),
                    feature=c("a", "c", "d", "e", "a"))
   getVennCounts(peaks1,peaks2)
   getVennCounts(peaks1,peaks2, by="feature")
   getVennCounts(peaks1, peaks2, by="base")
}
```

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HOT.spots

High Occupancy of Transcription Related Factors regions

### **Description**

High Occupancy of Transcription Related Factors regions of human (hg19)

### Usage

HOT.spots

#### **Format**

An object of GRangesList

#### **Details**

```
How to generated the data:
temp <- tempfile()
url <- "http://metatracks.encodenets.gersteinlab.org"
download.file(file.path(url, "HOT\_All\_merged.tar.gz"), temp)
temp2 <- tempfile()
download.file(file.path(url, "HOT_intergenic_All_merged.tar.gz"), temp2)
untar(temp, exdir=dirname(temp))
untar(temp2, exdir=dirname(temp))
f <- dir(dirname(temp), "bed$")
HOT.spots <- sapply(file.path(dirname(temp), f), toGRanges, format="BED")
names(HOT.spots) <- gsub("_merged.bed", "", f)
HOT.spots <- sapply(HOT.spots, unname)</pre>
HOT.spots <- GRangesList(HOT.spots)</pre>
save(list="HOT.spots",
file="data/HOT.spots.rda",
compress="xz", compression_level=9)
```

#### **Source**

http://metatracks.encodenets.gersteinlab.org/

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#### References

Yip KY, Cheng C, Bhardwaj N, Brown JB, Leng J, Kundaje A, Rozowsky J, Birney E, Bickel P, Snyder M, Gerstein M. Classification of human genomic regions based on experimentally determined binding sites of more than 100 transcription-related factors. Genome Biol. 2012 Sep 26;13(9):R48. doi: 10.1186/gb-2012-13-9-r48. PubMed PMID: 22950945; PubMed Central PM-CID: PMC3491392.

## **Examples**

```
data(HOT.spots)
elementNROWS(HOT.spots)
```

hyperGtest

hypergeometric test

## **Description**

hypergeometric test with lower.tail = FALSE used by getEnrichedGO

#### Usage

hyperGtest(alltermcount, thistermcount, totaltermInGenome, totaltermInPeakList)

#### **Arguments**

alltermcount a list with two variables: GOterm and GOcount which is GO terms and corre-

sponding counts in the whole genome

thistermcount a list with two variables: GOterm and GOcount which is GO terms and corre-

sponding counts in the peak list

totaltermInGenome

number of total GO terms in the whole genome

totaltermInPeakList

number of total GO terms in the peak list

## **Details**

see phyper for details

## Value

a list with 6 variables

thisterm GO term

thistermcount count of this GO term in the peak list

thistermtotal count of this GO term in the whole genome

74 IDRfilter

#### Note

internal function not intended to be used directly by users

## Author(s)

Lihua Julie ZHu

#### References

Johnson, N. L., Kotz, S., and Kemp, A. W. (1992) Univariate Discrete Distributions, Second Edition. New York: Wiley

#### See Also

phyper, getEnrichedGO

## **Examples**

**IDRfilter** 

Filter peaks by IDR (irreproducible discovery rate)

# Description

Using IDR to assess the consistency of replicate experiments and obtain a high-confidence single set of peaks

IDRfilter 75

## Usage

```
IDRfilter(
  peaksA,
  peaksB,
  bamfileA,
  bamfileB,
  maxgap = -1L,
  minoverlap = 0L,
  singleEnd = TRUE,
  IDRcutoff = 0.01,
  ...
)
```

# **Arguments**

```
peaksA, peaksB peaklist, GRanges object.

bamfileA, bamfileB
file path of bam files.

maxgap, minoverlap
Used in the internal call to findOverlaps() to detect overlaps. See ?findOverlaps in the IRanges package for a description of these arguments.

singleEnd (Default TRUE) A logical indicating if reads are single or paired-end.

IDRcutoff If the IDR no less than IDRcutoff, the peak will be removed.

... Not used.
```

#### Value

An object GRanges

## Author(s)

Jianhong Ou

#### References

Li, Qunhua, et al. "Measuring reproducibility of high-throughput experiments." The annals of applied statistics (2011): 1752-1779.

```
if(interactive()){
  path <- system.file("extdata", "reads", package="MMDiffBamSubset")
  if(file.exists(path)){
     bamfileA <- file.path(path, "reads", "WT_2.bam")
     bamfileB <- file.path(path, "reads", "Resc_2.bam")
     WT.AB2.Peaks <- file.path(path, "peaks", "WT_2_Macs_peaks.xls")
     Resc.AB2.Peaks <- file.path(path, "peaks", "Resc_2_Macs_peaks.xls")</pre>
```

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makeVennDiagram

Make Venn Diagram from a list of peaks

# Description

Make Venn Diagram from two or more peak ranges, Also calculate p-value to determine whether those peaks overlap significantly.

## Usage

```
makeVennDiagram(
   Peaks,
   NameOfPeaks,
   maxgap = -1L,
   minoverlap = 0L,
   totalTest,
   by = c("region", "feature", "base"),
   ignore.strand = TRUE,
   connectedPeaks = c("min", "merge", "keepAll", "keepFirstListConsistent"),
   method = c("hyperG", "permutation"),
   TxDb,
   plot = TRUE,
   ...
)
```

## **Arguments**

Peaks A list of peaks in GRanges format: See example below.

NameOfPeaks Character vector to specify the name of Peaks, e.g., c("TF1", "TF2"). This will

be used as label in the Venn Diagram.

maxgap, minoverlap

Used in the internal call to findOverlaps() to detect overlaps. See ?findOverlaps

in the **IRanges** package for a description of these arguments.

totalTest Numeric value to specify the total number of tests performed to obtain the list

of peaks. It should be much larger than the number of peaks in the largest peak

set.

make VennDiagram 77

by	"region", "feature" or "base", default = "region". "feature" means using feature field in the GRanges for calculating overlap, "region" means using chromosome range for calculating overlap, and "base" means calculating overlap in nucleotide level.
ignore.strand	Logical: when set to TRUE, the strand information is ignored in the overlap calculations.
connectedPeaks	If multiple peaks involved in overlapping in several groups, set it to "merge" will count it as only 1, while set it to "min" will count it as the minimal involved peaks in any connected peak group. "keepAll" will show all the original counts for each list while the final counts will be same as "min". "keepFirstListConsistent" will keep the counts consistent with first list.
method	method to be used for p value calculation. hyperG means hypergeometric test and permutation means peakPermTest.
TxDb	An object of TxDb.
plot	logical. If TRUE (default), a venn diagram is plotted.
	Additional arguments to be passed to venn.diagram.

#### **Details**

For customized graph options, please see venn.diagram in VennDiagram package.

#### Value

A p.value is calculated by hypergeometric test or permutation test to determine whether the overlaps of peaks or features are significant.

#### Author(s)

Lihua Julie Zhu, Jianhong Ou

#### See Also

findOverlapsOfPeaks, venn.diagram, peakPermTest

```
strand = c("+", "+", "-", "-", "+"),
                 feature=c("a","b","c","d","a"))
makeVennDiagram(list(peaks1, peaks2), NameOfPeaks=c("TF1", "TF2"),
                totalTest=100, scaled=FALSE, euler.d=FALSE,
                fill=c("#009E73", "#F0E442"), # circle fill color
                col=c("#D55E00", "#0072B2"), #circle border color
                cat.col=c("#D55E00", "#0072B2"))
makeVennDiagram(list(peaks1, peaks2), NameOfPeaks=c("TF1", "TF2"),
                totalTest=100,
                fill=c("#009E73", "#F0E442"), # circle fill color
                col=c("#D55E00", "#0072B2"), #circle border color
                cat.col=c("#D55E00", "#0072B2"))
###### 4-way diagram using annotated feature instead of chromosome ranges
makeVennDiagram(list(peaks1, peaks2, peaks1, peaks2),
                NameOfPeaks=c("TF1", "TF2", "TF3", "TF4"),
                totalTest=100, by="feature",
                main = "Venn Diagram for 4 peak lists",
                fill=c(1,2,3,4))
}
```

mergePlusMinusPeaks

Merge peaks from plus strand and minus strand

## **Description**

Merge peaks from plus strand and minus strand within certain distance apart, and output merged peaks as bed format.

# Usage

```
mergePlusMinusPeaks(
   peaks.file,
   columns = c("name", "chromosome", "start", "end", "strand", "count", "count", "count"),
   sep = "\t",
   header = TRUE,
   distance.threshold = 100,
   plus.strand.start.gt.minus.strand.end = TRUE,
   output.bedfile
)
```

#### **Arguments**

peaks.file Specify the peak file. The peak file should contain peaks from both plus and

minus strand

columns Specify the column names in the peak file

mergePlusMinusPeaks 79

sep Specify column delimiter, default tab-delimited

header Specify whether the file has a header row, default TRUE

distance.threshold

Specify the maximum gap allowed between the plus stranded and the nagative

stranded peak

plus.strand.start.gt.minus.strand.end

Specify whether plus strand peak start greater than the paired negative strand

peak end. Default to TRUE

output.bedfile Specify the bed output file name

#### Value

output the merged peaks in bed file and a data frame of the bed format

#### Author(s)

Lihua Julie Zhu

#### References

Zhu L.J. et al. (2010) ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIP-chip data. BMC Bioinformatics 2010, 11:237doi:10.1186/1471-2105-11-237

#### See Also

annotatePeakInBatch, findOverlappingPeaks, makeVennDiagram

80 metagenePlot

metagenePlot

peak distance to features

## Description

Bar plot for distance to features

## Usage

```
metagenePlot(
  peaks,
  AnnotationData,
  PeakLocForDistance = c("middle", "start", "end"),
  FeatureLocForDistance = c("TSS", "middle", "geneEnd"),
  upstream = 1e+05,
  downstream = 1e+05
)
```

## **Arguments**

peaks peak list, GRanges object or a GRangesList.

AnnotationData A GRanges object or a TxDb object.

PeakLocForDistance

Specify the location of peak for calculating distance,i.e., middle means using middle of the peak to calculate distance to feature, start means using start of the peak to calculate the distance to feature. To be compatible with previous version, by default using start

FeatureLocForDistance

Specify the location of feature for calculating distance,i.e., middle means using middle of the feature to calculate distance of peak to feature, TSS means using start of feature when feature is on plus strand and using end of feature when feature is on minus strand, geneEnd means using end of feature when feature is on plus strand and using start of feature when feature is on minus strand.

upstream, downstream

numeric(1). Upstream or downstream region of features to plot.

#### **Details**

the bar heatmap is indicates the peaks around features.

```
path <- system.file("extdata", package="ChIPpeakAnno")
files <- dir(path, "broadPeak")
peaks <- sapply(file.path(path, files), toGRanges, format="broadPeak")
peaks <- GRangesList(peaks)
names(peaks) <- sub(".broadPeak", "", basename(names(peaks)))</pre>
```

myPeakList 81

```
library(TxDb.Hsapiens.UCSC.hg19.knownGene)
metagenePlot(peaks, TxDb.Hsapiens.UCSC.hg19.knownGene)
```

myPeakList

An example GRanges object representing a ChIP-seq peak dataset

## **Description**

the putative STAT1-binding regions identified in un-stimulated cells using ChIP-seq technology (Robertson et al., 2007)

## Usage

myPeakList

#### **Format**

GRanges with slot rownames containing the ID of peak as character, slot start containing the start position of the peak, slot end containing the end position of the peak and sequames containing the chromosome where the peak is located.

#### Source

Robertson G, Hirst M, Bainbridge M, Bilenky M, Zhao Y, et al. (2007) Genome-wide profiles of STAT1 DNA association using chromatin immunoprecipitation and massively parallel sequencing. Nat Methods 4:651-7

## **Examples**

```
data(myPeakList)
slotNames(myPeakList)
```

oligoFrequency

get the oligonucleotide frequency

#### **Description**

Prepare the oligonucleotide frequency for given Markov order.

## Usage

```
oligoFrequency(sequence, MarkovOrder = 3L)
```

## **Arguments**

sequence The sequences packaged in DNAStringSet, DNAString object or output of func-

tion getAllPeakSequence.

MarkovOrder Markov order.

82 oligoSummary

## Value

A numeric vector.

#### Author(s)

Jianhong Ou

#### See Also

See Also as oligoSummary

#### **Examples**

```
library(seqinr)
library(Biostrings)
oligoFrequency(DNAString("AATTCGACGTACAGATGACTAGACT"))
```

oligoSummary

Output a summary of consensus in the peaks

## **Description**

Calculate the z-scores of all combinations of oligonucleotide in a given length by Markove chain.

## Usage

```
oligoSummary(
   sequence,
   oligoLength = 6L,
   freqs = NULL,
   MarkovOrder = 3L,
   quickMotif = FALSE,
   revcomp = FALSE,
   maxsize = 1e+05
)
```

#### **Arguments**

sequence The sequences packaged in DNAStringSet, DNAString object or output of func-

tion getAllPeakSequence.

oligoLength The length of oligonucleotide. freqs Output of function frequency. MarkovOrder The order of Markov chain.

quickMotif Generate the motif by z-score of not.

revcomp Consider both the given strand and the reverse complement strand when search-

ing for motifs in a complementable alphabet (ie DNA). Default, FALSE.

maxsize Maximum allowed dataset size (in length of sequences).

peakPermTest 83

## Value

A list is returned.

zscore A numeric vector. The z-scores of each oligonucleotide.

counts A numeric vector. The counts number of each oligonucleotide.

motifs a list of motif matrix.

## Author(s)

Jianhong Ou

#### References

van Helden, Jacques, Marcel li del Olmo, and Jose E. Perez-Ortin. "Statistical analysis of yeast genomic downstream sequences reveals putative polyadenylation signals." Nucleic Acids Research 28.4 (2000): 1000-1010.

#### See Also

See Also as frequency

# **Examples**

peakPermTest

Permutation Test for two given peak lists

## **Description**

Performs a permutation test to seee if there is an association between two given peak lists.

84 peakPermTest

#### Usage

```
peakPermTest(
  peaks1,
  peaks2,
  ntimes = 100,
  seed = as.integer(Sys.time()),
  mc.cores = getOption("mc.cores", 2L),
  maxgap = -1L,
  pool,
  TxDb,
  bindingDistribution,
  bindingType = c("TSS", "geneEnd"),
  featureType = c("transcript", "exon"),
  seqn = NA,
  ...
)
```

## Arguments

peaks1, peaks2 an object of GRanges ntimes number of permutations

seed random seed

mc. cores The number of cores to use. see mclapply.

maxgap See findOverlaps in the IRanges package for a description of these arguments.

pool an object of permPool

TxDb an object of TxDb

bindingDistribution

an object of bindist

bindingType where the peaks should bind, TSS or geneEnd

featureType what annotation type should be used for detecting the binding distribution.

seqn default is NA, which means not filter the universe pool for sampling. Otherwise

the universe pool will be filtered by the seqnames in seqn.

... further arguments to be passed to numOverlaps.

## Value

A list of class permTestResults. See permTest

#### Author(s)

Jianhong Ou

## References

Davison, A. C. and Hinkley, D. V. (1997) Bootstrap methods and their application, Cambridge University Press, United Kingdom, 156-160

## See Also

preparePool, bindist

## **Examples**

Peaks.Ste12.Replicate1

Ste12-binding sites from biological replicate 1 in yeast (see reference)

## **Description**

Ste12-binding sites from biological replicate 1 in yeast (see reference)

## Usage

```
Peaks.Ste12.Replicate1
```

## **Format**

GRanges with slot names containing the ID of peak as character, slot start containing the start position of the peak, slot end containing the end position of the peak and space containing the chromosome where the peak is located.

#### References

Philippe Lefranois, Ghia M Euskirchen, Raymond K Auerbach, Joel Rozowsky, Theodore Gibson, Christopher M Yellman, Mark Gerstein and Michael Snyder (2009) Efficient yeast ChIP-Seq using multiplex short-read DNA sequencing BMC Genomics 10:37

```
data(Peaks.Ste12.Replicate1)
Peaks.Ste12.Replicate1
```

Peaks.Ste12.Replicate2

Ste12-binding sites from biological replicate 2 in yeast (see reference)

# **Description**

Ste12-binding sites from biological replicate 2 in yeast (see reference)

#### Usage

Peaks.Ste12.Replicate2

#### **Format**

GRanges with slot names containing the ID of peak as character, slot start containing the start position of the peak, slot end containing the end position of the peak and space containing the chromosome where the peak is located.

#### Source

http://www.biomedcentral.com/1471-2164/10/37

## References

Philippe Lefranois, Ghia M Euskirchen, Raymond K Auerbach, Joel Rozowsky, Theodore Gibson, Christopher M Yellman, Mark Gerstein and Michael Snyder (2009) Efficient yeast ChIP-Seq using multiplex short-read DNA sequencing BMC Genomics 10:37doi:10.1186/1471-2164-10-37

## **Examples**

data(Peaks.Ste12.Replicate2)
Peaks.Ste12.Replicate2

Peaks.Ste12.Replicate3

*Ste12-binding sites from biological replicate 3 in yeast (see reference)* 

# Description

Ste12-binding sites from biological replicate 3 in yeast (see reference)

## Usage

Peaks.Ste12.Replicate3

peaks1 87

#### **Format**

GRanges with slot names containing the ID of peak as character, slot start containing the start position of the peak, slot end containing the end position of the peak and space containing the chromosome where the peak is located.

#### **Source**

http://www.biomedcentral.com/1471-2164/10/37

#### References

Philippe Lefranois, Ghia M Euskirchen, Raymond K Auerbach, Joel Rozowsky, Theodore Gibson, Christopher M Yellman, Mark Gerstein and Michael Snyder (2009) Efficient yeast ChIP-Seq using multiplex short-read DNA sequencing BMC Genomics 10:37doi:10.1186/1471-2164-10-37

## **Examples**

```
data(Peaks.Ste12.Replicate3)
Peaks.Ste12.Replicate3
```

peaks1

An example GRanges object representing a ChIP-seq peak dataset

# Description

An example GRanges object representing a ChIP-seq peak dataset

#### Usage

peaks1

#### **Format**

**GRanges** 

```
data(peaks1)
head(peaks1, n = 2)
```

88 peaks3

peaks2

An example GRanges object representing a ChIP-seq peak dataset

# Description

An example GRanges object representing a ChIP-seq peak dataset

# Usage

peaks2

## **Format**

GRanges

# **Examples**

```
data(peaks2)
head(peaks2, n = 2)
```

peaks3

An example GRanges object representing a ChIP-seq peak dataset

# Description

An example GRanges object representing a ChIP-seq peak dataset

# Usage

peaks3

## **Format**

GRanges

```
data(peaks3)
head(peaks3, n = 2)
```

peaksNearBDP 89

peaksNearBDP	obtain the peaks near bi-directional promoters	

## **Description**

Obtain the peaks near bi-directional promoters. Also output percent of peaks near bi-directional promoters.

#### Usage

```
peaksNearBDP(myPeakList, AnnotationData, MaxDistance = 5000L, ...)
```

#### **Arguments**

myPeakList GRanges: See example below

AnnotationData annotation data obtained from getAnnotation or customized annotation of class

GRanges containing additional variable: strand (1 or + for plus strand and -1 or -

for minus strand). For example, data(TSS.human.NCBI36), data(TSS.mouse.NCBIM37),

data(TSS.rat.RGSC3.4) and data(TSS.zebrafish.Zv8).

MaxDistance Specify the maximum gap allowed between the peak and nearest gene

. . . Not used

#### Value

#### A list of 4

list("peaksWithBDP")

annotated Peaks containing bi-directional promoters.

GRangesList with slot start holding the start position of the peak, slot end holding the end position of the peak, slot space holding the chromosome location where the peak is located, slot rownames holding the id of the peak. In addition, the following variables are included.

feature: id of the feature such as ensembl gene ID

insideFeature: upstream: peak resides upstream of the feature; downstream: peak resides downstream of the feature; inside: peak resides inside the feature; overlapStart: peak overlaps with the start of the feature; overlapEnd: peak overlaps with the end of the feature; includeFeature: peak include the feature entirely.

distance to Feature: distance to the nearest feature such as transcription start site. By default, the distance is calculated as the distance between the start of the binding site and the TSS that is the gene start for genes located on the forward strand and the gene end for genes located on the reverse strand. The user can specify the location of peak and location of feature for calculating this

feature\_range: start and end position of the feature such as gene

feature\_strand: 1 or + for positive strand and -1 or - for negative strand where the feature is located

90 permPool-class

#### Author(s)

Lihua Julie Zhu, Jianhong Ou

#### References

Zhu L.J. et al. (2010) ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIP-chip data. BMC Bioinformatics 2010, 11:237doi:10.1186/1471-2105-11-237

#### See Also

annotatePeakInBatch, findOverlappingPeaks, makeVennDiagram

## **Examples**

permPool-class

Class "permPool"

## **Description**

An object of class "permPool" represents the possible locations to do permutation test.

## Slots

```
grs object of "GRangesList" The list of binding ranges
N vector of "integer", permutation number for each ranges
```

pie1 91

#### **Objects from the Class**

Objects can be created by calls of the form new("permPool", grs="GRangesList", N="integer").

#### See Also

preparePool, peakPermTest

pie1

Pie Charts

## **Description**

Draw a pie chart with percentage

## Usage

```
pie1(
  х,
  labels = names(x),
  edges = 200,
  radius = 0.8,
  clockwise = FALSE,
  init.angle = if (clockwise) 90 else 0,
  density = NULL,
  angle = 45,
  col = NULL,
  border = NULL,
  lty = NULL,
 main = NULL,
  percentage = TRUE,
  rawNumber = FALSE,
  digits = 3,
  cutoff = 0.01,
  legend = FALSE,
  legendpos = "topright",
  legendcol = 2,
  radius.innerlabel = radius,
)
```

#### **Arguments**

Х

a vector of non-negative numerical quantities. The values in x are displayed as the areas of pie slices.

labels

one or more expressions or character strings giving names for the slices. Other objects are coerced by as.graphicsAnnot. For empty or NA (after coercion to character) labels, no label nor pointing line is drawn.

92 pie1

edges the circular outline of the pie is approximated by a polygon with this many

edges.

radius the pie is drawn centered in a square box whose sides range from -1 to 1. If the

character strings labeling the slices are long it may be necessary to use a smaller

radius.

clockwise logical indicating if slices are drawn clockwise or counter clockwise (i.e., math-

ematically positive direction), the latter is default.

init.angle number specifying the starting angle (in degrees) for the slices. Defaults to 0

(i.e., "3 o'clock") unless clockwise is true where init.angle defaults to 90 (de-

grees), (i.e., "12 o'clock").

density the density of shading lines, in lines per inch. The default value of NULL means

that no shading lines are drawn. Non-positive values of density also inhibit the

drawing of shading lines.

angle the slope of shading lines, given as an angle in degrees (counter-clockwise).

col a vector of colors to be used in filling or shading the slices. If missing a set of 6

pastel colours is used, unless density is specified when par("fg") is used.

border, 1ty (possibly vectors) arguments passed to polygon which draws each slice.

main an overall title for the plot.

percentage logical. Add percentage in the figure or not. default TRUE.

rawNumber logical. Instead percentage, add raw number in the figure or not. default FALSE.

digits When set percentage as TRUE, how many significant digits are to be used for

percentage. see format. default 3.

cutoff When percentage is TRUE, if the percentage is lower than cutoff, it will NOT

be shown. default 0.01.

legend logical. Instead of lable, draw legend for the pie. default, FALSE.

legendpos, legendcol

legend position and legend columns. see legend

radius.innerlabel

position of percentage or raw number label relative to the circle.

graphical parameters can be given as arguments to pie. They will affect the main

title and labels only.

#### Author(s)

Jianhong Ou

#### See Also

pie

# **Examples**

pie1(1:5)

plotBinOverRegions 93

plotBinOverRegions

plot the coverage of regions

# Description

plot the output of binOverRegions or binOverGene

## Usage

```
plotBinOverRegions(dat, ...)
```

## **Arguments**

dat

A list of matrix which indicate the coverage of regions per bin

. . .

Parameters could be used by matplot

## Author(s)

Jianhong Ou

#### See Also

binOverRegions, binOverGene

94 preparePool

preparePool

prepare data for permutation test

## **Description**

prepare data for permutation test peakPermTest

## Usage

```
preparePool(
   TxDb,
   template,
   bindingDistribution,
   bindingType = c("TSS", "geneEnd"),
   featureType = c("transcript", "exon"),
   seqn = NA
)
```

# Arguments

TxDb an object of TxDb template an object of GRanges bindingDistribution

an object of bindist

bindingType the relevant position to features featureType feature type, transcript or exon.

seqn seqnames. If given, the pool for permutation will be restrict in the given chro-

mosomes.

## Value

a list with two elements, grs, a list of GRanges. N, the numbers of elements should be drawn from in each GRanges.

## Author(s)

Jianhong Ou

## See Also

peakPermTest, bindist

reCenterPeaks 95

## **Examples**

reCenterPeaks

re-center the peaks

## **Description**

Create a new list of peaks based on the peak centers of given list.

# Usage

```
reCenterPeaks(peaks, width = 2000L, ...)
```

## **Arguments**

peaks An object of GRanges or annoGR.

width The width of new peaks

... Not used.

#### Value

An object of GRanges.

# Author(s)

Jianhong Ou

```
reCenterPeaks(GRanges("chr1", IRanges(1, 10)), width=2)
```

summarizeOverlapsByBins

Perform overlap queries between reads and genomic features by bins

## **Description**

summarizeOverlapsByBins extends summarizeOverlaps by providing fixed window size and step to split each feature into bins and then do queries. It will return counts by signalSummaryFUN, which applied to bins in one feature, for each feature.

## Usage

```
summarizeOverlapsByBins(
  targetRegions,
  reads,
  windowSize = 50,
  step = 10,
  signalSummaryFUN = max,
  mode = countByOverlaps,
  ...
)
```

# Arguments

targetRegions A GRanges object of genomic regions of interest.

reads A GRanges, GRangesList GAlignments, GAlignmentsList, GAlignmentPairs or

BamFileList object that represents the data to be counted by summarizeOverlaps.

windowSize Size of windows step Step of windows

signalSummaryFUN

function, which will be applied to the bins in each feature.

mode mode can be one of the pre-defined count methods. see summarizeOverlaps. de-

fault is countByOverlaps, alia of countOverlaps(features, reads, ignore.strand=ignore.strand)

... Additional arguments passed to summarizeOverlaps.

## Value

A RangedSummarizedExperiment object. The assays slot holds the counts, rowRanges holds the annotation from features.

## Author(s)

Jianhong Ou

summarizePatternInPeaks 97

#### **Examples**

summarizePatternInPeaks

Output a summary of the occurrence and enrichment of each pattern in the sequences.

## **Description**

Output a summary of the occurrence and enrichment of each pattern in the sequences.

#### Usage

```
summarizePatternInPeaks(
  patternFilePath,
  format = "fasta",
  BSgenomeName,
  peaks,
  revcomp = TRUE,
  method = c("binom.test", "permutation.test"),
  expectFrequencyMethod = c("Markov", "Naive"),
  MarkovOrder = 3L,
  bgdForPerm = c("shuffle", "chromosome"),
  chromosome = c("asPeak", "random"),
  nperm = 1000,
  alpha = 0.05,
  ...
)
```

#### **Arguments**

patternFilePath

Character value. The path to the file that contains the pattern.

format

Character value. The format of file containing the oligonucleotide pattern, either "fasta" (default) or "fastq".

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BSgenomeName Character value. BSgenome object. Please refer to available genomes in BSgenome

package for details.

peaks Character value. GRanges containing the peaks.

revcomp Boolean value, if TURE, also search the reverse compliment of pattern. Default

is TRUE.

method Character value. Method for pattern enrichment test, 'binom.test' (default) or

'permutation.test'.

expectFrequencyMethod

Character value. Method for calculating the expected probability of pattern oc-

currence, 'Markov' (default) or 'Naive'.

MarkovOrder Integer value. The order of Markov chain. Default is 3.

bgdForPerm Character value. The method for obtaining the background sequence. 'chro-

mosome' (default) selects background chromosome from chromosomes, refer to 'chromosome' parameter; 'shuffle' will obtain the backgroud sequence by

shufflubg any k-mers in peak sequences, refer to '...'.

chromosome Character value. Relevant if "bgdForPerm='chromosome'". 'asPeak' means to

use the same chromosomes in peaks; 'random' means to use all chromosomes

randomly. Default is 'asPeak'.

nperm Integer value. The number of permutation test, default is 1000.

alpha Numeric value. The significant level for permutation test, default is 0.05.

... Aditional parameter passed to function shuffle\_sequences

#### Details

Please see shuffle\_sequences for the more information bout 'shuffle' method.

#### Value

A list including two data frames named 'motif\_enrichment' and 'motif\_occurrence'. The 'motif\_enrichment' has four columns:

- "patternNum": number of matched pattern
- "totalNumPatternWithSameLen": total number of pattern with the same length
- "expectedRate": expected rate of pattern for 'binom.test' method
- "patternRate": real rate of pattern for 'permutation.test' method
- "pValueBinomTest": p value of bimom test for 'binom.test' method
- "cutOffPermutationTest": cut off of permutation test for 'permutation.test' method

The 'motif occurrence' has 14 columns:

- "motifChr": Chromosome of motif
- "motifStartInChr": motif start position in chromosome
- "motifEndInChr": motif end position in chromosome
- "motifName": motif name

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- "motifPattern": motif pattern
- "motifStartInPeak": motif start position in peak
- "motifEndInPeak": motif end position in peak
- "motifFound": specific motif Found in peak
- "motifFoundStrand": strand of specific motif Found in peak, "-" means reverse complement of motif found in peaks
- "peakChr": Chromosome of peak
- "peakStart": peak start position
- "peakEnd": peak end position
- "peakWidth": peak width
- "peakStrand": peak strand

## Author(s)

Lihua Julie Zhu, Junhui Li, Kai Hu

## **Examples**

tileCount

Perform overlap queries between reads and genome by windows

## **Description**

tileCount extends summarizeOverlaps by providing fixed window size and step to split whole genome into windows and then do queries. It will return counts in each windows.

```
tileCount(
  reads,
  genome,
  windowSize = 1e+06,
  step = 1e+06,
  keepPartialWindow = FALSE,
  mode = countByOverlaps,
  ...
)
```

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# **Arguments**

reads A GRanges, GRangesList GAlignments, GAlignmentsList, GAlignmentPairs or

BamFileList object that represents the data to be counted by summarizeOverlaps.

genome The object from/on which to get/set the sequence information.

windowSize Size of windows step Step of windows

keepPartialWindow

Keep last partial window or not.

mode can be one of the pre-defined count methods. see summarizeOverlaps. de-

fault is countByOverlaps, alia of countOverlaps(features, reads, ignore.strand=ignore.strand)

... Additional arguments passed to summarizeOverlaps.

#### Value

A RangedSummarizedExperiment object. The assays slot holds the counts, rowRanges holds the annotation from genome.

#### Author(s)

Jianhong Ou

## **Examples**

tileGRanges

Slide windows on a given GRanges object

## **Description**

tileGRanges returns a set of genomic regions by sliding the windows in a given step. Each window is called a "tile".

```
tileGRanges(targetRegions, windowSize, step, keepPartialWindow = FALSE, ...)
```

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## Arguments

```
targetRegions A GRanges object of genomic regions of interest.

windowSize Size of windows

step Step of windows

keepPartialWindow

Keep last partial window or not.

... Not used.
```

#### Value

A GRanges object.

## Author(s)

Jianhong Ou

## **Examples**

toGRanges

Convert dataset to GRanges

# Description

Convert UCSC BED format and its variants, such as GFF, or any user defined dataset such as MACS output file to GRanges

```
toGRanges(data, ...)
## S4 method for signature 'connection'
toGRanges(
  data,
  format = c("BED", "GFF", "GTF", "MACS", "MACS2", "MACS2.broad", "narrowPeak",
        "broadPeak", "CSV", "others"),
  header = FALSE,
  comment.char = "#",
```

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```
colNames = NULL,
)
## S4 method for signature 'TxDb'
toGRanges(
 data,
 feature = c("gene", "transcript", "exon", "CDS", "fiveUTR", "threeUTR", "microRNA",
    "tRNAs", "geneModel"),
 OrganismDb,
)
## S4 method for signature 'EnsDb'
toGRanges(
  data,
  feature = c("gene", "transcript", "exon", "disjointExons"),
)
## S4 method for signature 'character'
toGRanges(
  data,
  format = c("BED", "GFF", "GTF", "MACS", "MACS2", "MACS2.broad", "narrowPeak",
    "broadPeak", "CSV", "others"),
  header = FALSE,
  comment.char = "#",
  colNames = NULL,
)
```

## **Arguments**

data an object of data.frame, TxDb or EnsDb, or the file name of data to be imported.

Alternatively, data can be a readable txt-mode connection (See ?read.table).

... parameters passed to read.table

format data format. If the data format is set to BED, GFF, narrowPeak or broadPeak,

please refer to http://genome.ucsc.edu/FAQ/FAQformat#format1 for column order. "MACS" is for converting the excel output file from MACS1. "MACS2" is for converting the output file from MACS2. If set to CSV, must have columns:

seqnames, start, end, strand.

header A logical value indicating whether the file contains the names of the variables as

its first line. If missing, the value is determined from the file format: header is set to TRUE if the first row contains one fewer field than the number of columns

or the format is set to 'CSV'.

comment.char character: a character vector of length one containing a single character or an

empty string. Use "" to turn off the interpretation of comments altogether.

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colNames If the data format is set to "others", colname must be defined. And the colname

must contain space, start and end. The column name for the chromosome #

should be named as space.

feature annotation type

OrganismDb an object of OrganismDb. It is used for extracting gene symbol for geneModel

group for TxDb

#### Value

An object of GRanges

## Author(s)

Jianhong Ou

```
macs <- system.file("extdata", "MACS_peaks.xls", package="ChIPpeakAnno")</pre>
macsOutput <- toGRanges(macs, format="MACS")</pre>
if(interactive() || Sys.getenv("USER")=="jianhongou"){
  ## MACS connection
 macs <- readLines(macs)</pre>
 macs <- textConnection(macs)</pre>
 macsOutput <- toGRanges(macs, format="MACS")</pre>
 close(macs)
  ## bed
  toGRanges(system.file("extdata", "MACS_output.bed", package="ChIPpeakAnno"),
              format="BED")
  ## narrowPeak
  toGRanges(system.file("extdata", "peaks.narrowPeak", package="ChIPpeakAnno"),
              format="narrowPeak")
  ## broadPeak
  toGRanges(system.file("extdata", "TAF.broadPeak", package="ChIPpeakAnno"),
              format="broadPeak")
  ## CSV
  toGRanges(system.file("extdata", "peaks.csv", package="ChIPpeakAnno"),
              format="CSV")
  ## MACS2
  toGRanges(system.file("extdata", "MACS2_peaks.xls", package="ChIPpeakAnno"),
              format="MACS2")
  toGRanges(system.file("extdata", "GFF_peaks.gff", package="ChIPpeakAnno"),
              format="GFF")
  ## EnsDb
  library(EnsDb.Hsapiens.v75)
  toGRanges(EnsDb.Hsapiens.v75, feature="gene")
  library(TxDb.Hsapiens.UCSC.hg19.knownGene)
  toGRanges(TxDb.Hsapiens.UCSC.hg19.knownGene, feature="gene")
  ## data.frame
  macs <- system.file("extdata", "MACS_peaks.xls", package="ChIPpeakAnno")</pre>
```

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```
macs <- read.delim(macs, comment.char="#")
toGRanges(macs)
}</pre>
```

translatePattern

translate pattern from IUPAC Extended Genetic Alphabet to regular expression

# Description

translate pattern containing the IUPAC nucleotide ambiguity codes to regular expression. For example, Y->[C|T], R-> [A|G], S-> [G|C], W-> [A|T], K-> [T|U|G], M-> [A|C], B-> [C|G|T], D-> [A|C|T], V-> [A|C|G] and N-> [A|C|T|G].

## Usage

```
translatePattern(pattern)
```

## **Arguments**

pattern

a character vector with the IUPAC nucleotide ambiguity codes

# Value

a character vector with the pattern represented as regular expression

#### Author(s)

Lihua Julie Zhu

#### See Also

countPatternInSeqs, summarizePatternInPeaks

```
pattern1 = "AACCNWMK"
translatePattern(pattern1)
```

TSS.human.GRCh37

TSS.human.GRCh37

TSS annotation for human sapiens (GRCh37) obtained from biomaRt

#### **Description**

TSS annotation for human sapiens (GRCh37) obtained from biomaRt

## Usage

TSS.human.GRCh37

#### **Format**

A GRanges object with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot sequames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
The dataset TSS.human.GRCh37 was obtained by:

mart = useMart(biomart = "ENSEMBL_MART_ENSEMBL", host="grch37.ensembl.org", path="/biomart/martservice",
dataset = "hsapiens_gene_ensembl")

getAnnotation(mart, featureType = "TSS")
```

## **Examples**

```
data(TSS.human.GRCh37)
slotNames(TSS.human.GRCh37)
```

TSS.human.GRCh38

TSS annotation for human sapiens (GRCh38) obtained from biomaRt

## **Description**

TSS annotation for human sapiens (GRCh38) obtained from biomaRt

# Usage

TSS.human.GRCh38

## Format

A 'GRanges' [package "GenomicRanges"] object with ensembl id as names.

TSS.human.NCBI36

#### **Details**

```
used in the examples Annotation data obtained by:

mart = useMart(biomart = "ensembl", dataset = "hsapiens_gene_ensembl")

getAnnotation(mart, featureType = "TSS")
```

## **Examples**

```
data(TSS.human.GRCh38)
slotNames(TSS.human.GRCh38)
```

TSS.human.NCBI36

TSS annotation for human sapiens (NCBI36) obtained from biomaRt

# Description

TSS annotation for human sapiens (NCBI36) obtained from biomaRt

## Usage

TSS.human.NCBI36

#### **Format**

GRanges with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot sequames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
used in the examples Annotation data obtained by:

mart = useMart(biomart = "ensembl_mart_47", dataset = "hsapiens_gene_ensembl", archive=TRUE)

getAnnotation(mart, featureType = "TSS")
```

```
data(TSS.human.NCBI36)
slotNames(TSS.human.NCBI36)
```

TSS.mouse.GRCm38

TSS.mouse.GRCm38	TSS annotation data for Mus musculus (GRCm38.p1) obtained from biomaRt
	biomaRt

## **Description**

TSS annotation data for Mus musculus (GRCm38.p1) obtained from biomaRt

#### Usage

TSS.mouse.GRCm38

#### **Format**

GRanges with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot seqnames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
Annotation data obtained by:

mart = useMart(biomart = "ensembl", dataset = "mmusculus_gene_ensembl")

getAnnotation(mart, featureType = "TSS")
```

#### **Examples**

```
data(TSS.mouse.GRCm38)
slotNames(TSS.mouse.GRCm38)
```

TSS.mouse.NCBIM37

TSS annotation data for mouse (NCBIM37) obtained from biomaRt

## **Description**

TSS annotation data for mouse (NCBIM37) obtained from biomaRt

## Usage

TSS.mouse.NCBIM37

TSS.rat.RGSC3.4

#### **Format**

GRanges with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot sequames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
Annotation data obtained by:

mart = useMart(biomart = "ensembl", dataset = "mmusculus_gene_ensembl")

getAnnotation(mart, featureType = "TSS")
```

## **Examples**

```
data(TSS.mouse.NCBIM37)
slotNames(TSS.mouse.NCBIM37)
```

TSS.rat.RGSC3.4

TSS annotation data for rat (RGSC3.4) obtained from biomaRt

## **Description**

TSS annotation data for rat (RGSC3.4) obtained from biomaRt

## Usage

```
TSS.rat.RGSC3.4
```

#### **Format**

GRanges with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot sequames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
Annotation data obtained by:

mart = useMart(biomart = "ensembl", dataset = "rnorvegicus_gene_ensembl")

getAnnotation(mart, featureType = "TSS")
```

```
data(TSS.rat.RGSC3.4)
slotNames(TSS.rat.RGSC3.4)
```

TSS.rat.Rnor\_5.0 109

## **Description**

TSS annotation data for Rattus norvegicus (Rnor\_5.0) obtained from biomaRt

## Usage

```
TSS.rat.Rnor_5.0
```

#### **Format**

GRanges with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot seqnames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
Annotation data obtained by:

mart = useMart(biomart = "ensembl", dataset = "rnorvegicus_gene_ensembl")

getAnnotation(mart, featureType = "TSS")
```

#### **Examples**

```
data(TSS.rat.Rnor_5.0)
slotNames(TSS.rat.Rnor_5.0)
```

TSS.zebrafish.Zv8

TSS annotation data for zebrafish (Zv8) obtained from biomaRt

## **Description**

A GRanges object to annotate TSS for zebrafish (Zv8) obtained from biomaRt

```
TSS.zebrafish.Zv8
```

110 TSS.zebrafish.Zv9

#### **Format**

GRanges with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot sequames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
Annotation data obtained by: mart <- useMart(biomart="ENSEMBL_MART_ENSEMBL", host="may2009.archive.ensemble path="/biomart/martservice", dataset="drerio_gene_ensembl")
getAnnotation(mart, featureType = "TSS")
```

#### **Examples**

```
data(TSS.zebrafish.Zv8)
slotNames(TSS.zebrafish.Zv8)
```

TSS.zebrafish.Zv9

TSS annotation for Danio rerio (Zv9) obtained from biomaRt

## **Description**

TSS annotation for Danio rerio (Zv9) obtained from biomaRt

## Usage

```
TSS.zebrafish.Zv9
```

## **Format**

GRanges with slot start holding the start position of the gene, slot end holding the end position of the gene, slot names holding ensembl gene id, slot sequames holding the chromosome location where the gene is located and slot strand holding the strinad information. In addition, the following variables are included.

list("description") description of the gene

#### **Details**

```
Annotation data obtained by:
```

```
mart <- useMart(biomart="ENSEMBL_MART_ENSEMBL", host="mar2015.archive.ensembl.org", path="/biomart/martservice", dataset="drerio_gene_ensembl")
getAnnotation(mart, featureType = "TSS")
```

TxDb2GR

## **Examples**

```
data(TSS.zebrafish.Zv9)
slotNames(TSS.zebrafish.Zv9)
```

TxDb2GR

TxDb object to GRanges

# Description

convert TxDb object to GRanges

# Usage

TxDb2GR(ranges, feature, OrganismDb)

# **Arguments**

ranges an Txdb object

feature feature type, could be geneModel, gene, exon, transcript, CDS, fiveUTR, three-

UTR, microRNA, and tRNA

OrganismDb org db object

wgEncodeTfbsV3

transcription factor binding site clusters (V3) from ENCODE

## **Description**

possible binding pool for human (hg19) from transcription factor binding site clusters (V3) from ENCODE data and removed the HOT spots

# Usage

wgEncodeTfbsV3

#### **Format**

An object of GRanges.

wgEncodeTfbsV3

#### **Details**

```
How to generate the data:
temp <- tempfile()
download.file(file.path("http://hgdownload.cse.ucsc.edu", "goldenPath",
"hg19", "encodeDCC",
"wgEncodeRegTfbsClustered",
"wgEncodeRegTfbsClusteredV3.bed.gz"), temp)
data <- read.delim(gzfile(temp, "r"), header=FALSE)
unlink(temp)
colnames(data)[1:4] <- c("seqnames", "start", "end", "TF")
wgEncodeRegTfbsClusteredV3 <- GRanges(as.character(data$seqnames),
IRanges(data$start, data$end),
TF=data$TF)
data(HOT.spots)
hot <- reduce(unlist(HOT.spots))</pre>
ol <- findOverlaps(wgEncodeRegTfbsClusteredV3, hot)
wgEncodeTfbsV3 <- wgEncodeRegTfbsClusteredV3[-unique(queryHits(ol))]
wgEncodeTfbsV3 <- reduce(wgEncodeTfbsV3)
save(list="wgEncodeTfbsV3",
file="data/wgEncodeTfbsV3.rda",
compress="xz", compression_level=9)
```

#### Source

http://hgdownload.cse.ucsc.edu/goldenPath/hg19/encodeDCC/wgEncodeRegTfbsClustered/wgEncodeRegTfbsClusteredV3

```
data(wgEncodeTfbsV3)
head(wgEncodeTfbsV3)
```

write2FASTA 113

write2FASTA	Write sequences to a file in fasta format	

## **Description**

Write the sequences obtained from getAllPeakSequence to a file in fasta format leveraging write-FASTA in Biostrings package. FASTA is a simple file format for biological sequence data. A FASTA format file contains one or more sequences and there is a header line which begins with a > proceeding each sequence.

# Usage

```
write2FASTA(mySeq, file = "", width = 80)
```

# Arguments

mySeq	GRanges with varibles name and sequence ,e.g., results obtained from getAll-PeakSequence
file	Either a character string naming a file or a connection open for reading or writing. If "" (the default for write2FASTA), then the function writes to the standard output connection (the console) unless redirected by sink
width	The maximum number of letters per line of sequence

#### Value

Output as FASTA file format to the naming file or the console.

#### Author(s)

Lihua Julie Zhu

```
peaksWithSequences = GRanges(seqnames=c("1", "2"),
IRanges(start=c(1000, 2000),
end=c(1010, 2010),
names=c("id1", "id2")),
sequence= c("CCCCCCCGGGGG", "TTTTTTTTAAAAAA"))
write2FASTA(peaksWithSequences, file="testseq.fasta", width=50)
```

114 xget

xget

Return the value from a Bimap objects

# Description

Search by name for an Bimap object.

# Usage

```
xget(
  x,
  envir,
  mode,
  ifnotfound = NA,
  inherits,
  output = c("all", "first", "last")
)
```

# Arguments

```
x, envir, mode, ifnotfound, inherits  \frac{\text{see mget}}{\text{output}}  output return the all or first item for each query
```

## Value

a character vector

# Author(s)

Jianhong Ou

## See Also

```
See Also as mget, mget
```

```
library(org.Hs.eg.db)
xget(as.character(1:10), org.Hs.egSYMBOL)
```

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