Package 'rtfbsdb'

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Title Parse TF motifs from public databases, read into R, and scan using 'rtfbs'.

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Depends R (>= 2.6)

Imports rphast, rtfbs, bigWig, parallel, grid, cluster, methods, latticeExtra, lattice

LinkingTo

Suggests RCurl, stringr

Description
Convenience functions to read and scan DNA sequences using Position Weight Matrices (PWMs)

License GPL version 3 or newer

biocViews Sequencing, Analysis

LazyLoad yes

R topics documented:

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`CisBP.db-class` *Class* `"CisBP.db"`

Description

The motif library from CisBP web site.
Link: `http://cisbp.ccbr.utoronto.ca/`

Objects from the Class

Objects can be created by calls of the form `CisBP.extdata`, `CisBP.zipload`, `CisBP.download`.

Slots

`species`: String indicating the species name defined in the CisBP dataset.

`zip.file`: String indicating the filename of temporary data file.

`zip.url`: String indicating the download source.

`file.tfinfo`: String indicating the TF filename, defulat is TF_Information.txt.

Extends

Class `"tfbs.db"`, directly.

Methods

tfbs.createFromCisBP Build a tfbs object by querying the meta file of CisBP dataset and subsetting the results.

CisBP.group Get the statistical summary by grouping the field in the CisBP dataset.

References

Weirauch, M. T., Yang, A., Albu, M., Cote, A. G., Montenegro-Montero, A., Drewe, P., ... & Hughes, T. R. (2014). Determination and inference of eukaryotic transcription factor sequence specificity. Cell, 158(6), 1431-1443.

See Also

`CisBP.group`, `tfbs.createFromCisBP`

Examples

```
showClass("CisBP.db")
```

`CisBP.download` *Download CisBP dataset.*

Description

Download TF data file from CisBP dataset and store it to temporary folder

Usage

```
CisBP.download(species = "Homo_sapiens",
      url = "http://cisbp.ccbr.utoronto.ca/bulk_archive.php")
```

Arguments

`species`	String, indicating the species name in the CisBP dataset
`url`	String, the URL of bulk dowbnloads from CisBP dataset, default is `http://cisbp.ccbr.utoronto.ca/bulk_archive.php`

Details

The dowload function has been confirmed in the web site of *cisbp.ccbr.utoronto.ca* o June, 2015.

Value

A CisBP object (class name: "`CisBP.db`") is returned with four items:

`species`	String indicating the species name
`zip.file`	String indicating the filename of temporary data file.
`zip.url`	String indicating the download source
`file.tfinfo`	String indicating the TF filename, default is TF_Information.txt.

References

Weirauch, M. T., Yang, A., Albu, M., Cote, A. G., Montenegro-Montero, A., Drewe, P., ... & Hughes, T. R. (2014). Determination and inference of eukaryotic transcription factor sequence specificity. Cell, 158(6), 1431-1443.

See Also

See Also as `CisBP.ziplload`, `CisBP.extdata`.

Examples

```
#download human dataset
db1 <- CisBP.download("Homo_sapiens");

#download mouse dataset
db2 <- CisBP.download("Mus_musculus");
```

`CisBP.extdata` *Load internal CisBP dataset.*

Description

Build a CisBP object from the internal zip file stored in this package

Usage

```
CisBP.extdata(species)
```

Arguments

`species`	String, only valid for human and mouse species, i.e. Homo_sapiens or Mus_musculus

Details

The CisBP data for Homo_sapiens and Mus_musculus are delivered by this package. When you use the newest dataset, you should download it from the website by `CisBP.download`.

Value

A CisBP object (class name: `"CisBP.db"`) is returned with four items:

`species`	String indicating the species name defined in the CisBP dataset.
`zip.file`	String indicating the filename of temporary data file.
`zip.url`	String indicating the download source
`file.tfinfo`	String indicating the TF filename, default is TF_Information.txt.

See Also

See Also as `CisBP.zipload`, `CisBP.download`.

Examples

```
#reading data from inner file
db.human <- CisBP.extdata("Homo_sapiens")
```

`CisBP.group` *Summarize the motif number.*

Description

Get the statistical summary by grouping the field in the CisBP dataset.

Usage

```
CisBP.group(cisbp.db,
      group.by=c("tf_name", "tf_species", "tf_status", "family_name",
            "motif_type", "msource_id"),
      tf.information.type=1)
```

Arguments

`cisbp.db`	A CisBP object ("`CisBP.db`") including the TF_Information.txt.
`group.by`	String, indicating which field will be used to group values. Available values are tf_name, tf_species, tf_status, family_name, motif_type and msource_id.
`tf.information.type`	Number, indicating which TF meta file will be used. Available values are 1 for TF_Information.txt, 2 for TF_Information_all_motifs.txt and 3 for F_Information_all_motifs_plus.txt.

Details

Three TF information files in CisBP dataset.

1: TF_Information.txt : (direct motifs) or (no direct but inferred motifs with 90%)
2: TF_Information_all_motifs.txt: (direct motifs) and (inferred motifs above the threshold)
3: F_Information_all_motifs_plus.txt: All motifs

Value

A data frame returned includes two columns

`group_by`	Values of grouping field
`number`	Counts of group value

See Also

See Also as `tfbs.createFromCisBP`

Examples

```
# Load the internal CisBP dataset
db_human <- CisBP.extdata("Homo_sapiens");

# Group the motif count by the column of family_name in TF_Information.txt
gr1 <- CisBP.group(db_human, group.by="family_name", tf.information.type=1 );
```

```
# Group the motif count by the column of tf_status in TF_Information.txt
gr2 <- CisBP.group(db_human, group.by="tf_status", tf.information.type=1 );

# Group the motif count by the column of tf_status in TF_Information_all_motifs.txt
gr3 <- CisBP.group(db_human, group.by="tf_status", tf.information.type=2);

# Group the motif count by the column of tf_status in F_Information_all_motifs_plus.txt
gr4 <- CisBP.group(db_human, group.by="tf_status", tf.information.type=3);
```

`CisBP.ziploadLoad the zipped CisBP file.`

Description

Build a CisBP object from the zipped CisBP file.

Usage

```
CisBP.zipload(zip.file, species = "Homo_sapiens")
```

Arguments

`zip.file`	String, indicating the zipped file data
`species`	String, indicating the species name in the CisBP database

Details

The zip data canbe downloaded from the web site, please check `CisBP.download`.

Value

A CisBP object (class name: `"CisBP.db"`) is returned with four items:

`species`	String indicating the species name
`zip.file`	String indicating the filename of temporary data file.
`zip.url`	String indicating the download source
`file.tfinfo`	String indicating the TF filename, default is TF_Information.txt.

See Also

See Also as `CisBP.extdata`, `CisBP.download`.

Examples

```
# Download the dataset
db2 <- CisBP.download("Mus_musculus");

# Loading the zip file, the db2 and db3 have same TF data.
# Here is an example to show how to use CisBP.zipload.
# We dont nee to download it by CisBP.download and then load it by CisBP.zipload
db3 <- CisBP.zipload(db2@zip.file, species="Mus_musculus");
```

print.tfbs.comparson *Print the brief comparson results*

Description

Print the brief comparson results.

Usage

```
## S3 method for class 'tfbs.comparson'
print(x, ..., pv.cutoff=0.05, pv.adj=NA )
```

Arguments

x	The result obtained by tfbs.compareTFsite.
...	Additional arguments affecting the print produced.
pv.cutoff	Numeric value,indicating whether the different cutoff of p-value is applied to select the significant motifs.
pv.adj	String, P-values correct method for p.adjust function. The available values are "holm", "hochberg", "hommel", "bonferroni", "BH", "BY","fdr" or "none".(default="bonferroni")

Details

This command shows the calling parameters and significant motifs from the result object.
The significant motifs are selected by the corrected p-value cutoff(0.05) and at most 20 significant motifs are listed. The adjust method of p-value is defined in the calling function.

Value

No return values.

See Also

See also as tfbs.compareTFsite.

Examples

```
#See example in tfbs.compareTFsite
```

print.tfbs.finding *Print scanning result of TF sites.*

Description

Print scanning result of TF sites.

Usage

```
## S3 method for class 'tfbs.finding'
print(x, ...)
```

Arguments

x	The result obtained by tfbs.scanTFsite.
...	Additional arguments affecting the print produced.

Details

This function shows a brief information including calling parameters and enriched motifs.

Value

No return values.

See Also

See Also as tfbs.scanTFsite

Examples

```
#See example in tfbs.scanTFsite
```

summary.tfbs.comparson *Summarize the comparson result*

Description

Return the significant motifs based on the adjust p-values using multiple comparisons.

Usage

```
## S3 method for class 'tfbs.comparson'
summary(object, pv.cutoff = 0.05, pv.adj = NA, ...)
```

Arguments

object	The result obtained by tfbs.compareTFsite.
pv.cutoff	The p-value cutoff for significant motifs.
pv.adj	P-values adjust method for p.adjust function. The available values are "holm", "hochberg", "hommel", "bonferroni", "BH", "BY","fdr" or "none".
...	Additional arguments affecting the summary produced.

Details

A data frame with 6 colums is returned.

Value

The results is a data frame including 6 columns,

motif.id	Motif ID
tf.name	TF Name
Npos	Read count in positive loci.
Nneg	Read count in negative loci.
pv.adj	p-value
es.ratio	The ratio of read counts between positive loci and negative loci.

See Also

See also as tfbs.compareTFsite.

---

summary.tfbs.finding

Summarize scanning results.

Description

Return a data frame with summarized TF sites for every motif if the calling parameter is "matches".

Usage

```
## S3 method for class 'tfbs.finding'
summary(object, ...)
```

Arguments

object	The result obtained by tfbs.scanTFsite.
...	Additional arguments affecting the summary produced.

Details

summary in class of tfbs.finding is returned.

Value

This function will return a data frame with summarized TF sites for every motif if the calling parameter is "matches", otherwise, NULL will be returned.

See Also

See Also as `tfbs.scanTFsite`

`tfbs` *Create a tfbs object from the supplied PWM files.*

Description

Create a tfbs object from the supplied PWM files.

Usage

```
tfbs(filenames,
      names,
      species="Homo_sapiens",
      extra_info = NULL, ...)
```

Arguments

`filenames`	Vector of PWM files
`names`	Vector of unique gene symbols.
`species`	String indicating species name
`extra_info`	Data frame including meta information for all motifs., Default: NULL
`...`	Parameters,such as pseudocount, force_even, and the parameters used in read.table function.

Details

Load the PWM files to build a `"tfbs"` object.

Value

A tfbs object (class: `"tfbs"`) including all PWM matrics.The all attributes are as follows:

`TFID`	Vector of non-unique ID for TF.
`species`	String indicating the species name
`ntfs`	Number of motifs in matrix.
`pwm`	A list including PWM matics.
`filename`	Vector of PWM filename.
`mgisymbols`	Unique gene symbols for TF.
`extra_info`	Data frame, including extra information for PWMs, it maybe different with motif dataset, default:NULL.

distancematrix
: Distance matrix between motifs returned by tfbs.getDistanceMatrix, default:NULL.

expressionlevel
: Data frame indicatig the result of expression level returned by tfbs.getExpression, default:NULL.

The tfbs object can be created by the function of tfbs, tfbs.dirs, tfbs.createFromCisBP.

See Also

tfbs, tfbs.dirs, tfbs.createFromCisBP

Examples

```
# M3590_1.01 PAX5 ENSG00000196092
# M3590_1.01 PAX5 ENSG00000196092
fs1 <- system.file("extdata","M3590_1.01.pwm", package="rtfbsdb")
fs2 <- system.file("extdata","M3591_1.01.pwm", package="rtfbsdb")

cat(fs1, "\n");

tfs <- tfbs( c( fs1, fs2 ), names=c("M3590_1.01","M3591_1.01"),
      header=TRUE, sep="\t" , row.names=1 );
str(tfs);
```

---

tfbs-class *Class* "tfbs"

Description

Tfbs object is a collection of motif PWM data. Some functions are provided based on the PWM and GENCODE data, such as clustering, search and compare.

Objects from the Class

Objects can be created by calls of the function of tfbs.createFromCisBP, tfbs.dirs and tfbs.

Slots

TFID Vector of non-unique ID for TF.

species String indicating the species name

ntfs Number of motifs in matrix.

pwm A list including PWM matics.

filename Vector of PWM filename.

mgisymbols Unique gene symbols for TF.

extra_info Data frame, including extra information for PWMs, it maybe different with motif dataset, default:NULL.

distancematrix Distance matrix between motifs returned by `tfbs.getDistanceMatrix`, default:NULL.

expressionlevel Data frame indicatig the result of expression level returned by `tfbs.getExpression`, default:NULL.

Methods

tfbs.getDistanceMatrix Calcuate a distance matrix with Pearson's R values

tfbs.getExpression Estimate gene expression of target TF.

tfbs.clusterMotifs Cluster the specified motifs and drawing the heatmap.

tfbs.scanTFsite Find TF sites from genome data within the BED ranges.

tfbs.compareTFsite Comparative TFBS search with the BED ranges

tfbs.selectByGeneExp Select the motifs with minimum p-value from each group of clustering.

tfbs.selectByRandom Select the motifs randomly from each group of clustering.

tfbs.drawLogosForClusters Draw the motif logos by one group per page.

tfbs.drawLogo Draw the logo for a single TF motif.

See Also

The class definition of tfbs.

Examples

```
showClass("tfbs")
```

`tfbs.clusterMotifs` *Clustering the specified motifs and drawing the heatmap.*

Description

Clustering the specified motifs and drawing the heatmap.

Usage

```
tfbs.clusterMotifs(tfbs,
      subset = NA,
      pdf.heatmap = NA,
      method = NA,
      group.k = NA)
```

Arguments

`tfbs`	A tfbs object (`"tfbs"`) returned by `tfbs.createFromCisBP`, `tfbs.dirs` or other functions.
`subset`	Vector, the indexes of partial motifs if not all motifs are clustered.
`pdf.heatmap`	String, a PDF filename for heatmap.
`method`	String, availabe values are "agnes" and "cors".
`group.k`	Integer, if the method of agnes is used to do clustering, the parameter of k is optional to use as preset group number.

Details

This result of clustering will be used in the

Value

A matrix with 2 columns is returned, 1st column is the index of motifs and 2nd column is the group number of clustering.

See Also

See Also as `tfbs.selectByGeneExp` and `tfbs.selectByRandom`

Examples

```
# Load the internal CisBP data set
db <- CisBP.extdata("Homo_sapiens");

# Create a tfbs object by querying the meta file of CisBP dataset.
tfs <- tfbs.createFromCisBP(db, motif_type="ChIP-seq", tf.information.type=1 );

# Calculate the distance matrix
tfs <- tfbs.getDistanceMatrix( tfs, ncores=1 );

# Cluster the motifs using the "cors" method
cluster1 <- tfbs.clusterMotifs(tfs, pdf.heatmap = "test-heatmap1.pdf", method="agnes" );
show(cluster1);

# draw motif logos on one group per page.
tfbs.drawLogosForClusters(tfs, cluster1, "test-cluster1.pdf");
```

`tfbs.compareTFsite` *Comparative TS sites between positive and negative TRE loci*

Description

Comparative TS sites between positive and negative TRE loci for all motifs.

Usage

```
tfbs.compareTFsite(tfbs,
      file.twoBit,
      positive.bed,
      negative.bed,
      file.prefix=NA,
      usecluster=NA,
      ncores=3,
      gc.correction=FALSE,
      fdr=0.1,
      threshold=NA,
      gc.groups=4,
```

```
        background.order=2,
        background.length=100000,
        pv.adj = p.adjust.methods)
```

Arguments

tfbs	A tfbs object, see also "tfbs"
file.twoBit	String, the file name of genome data(e.g. hg19.2bit, mm10.2bit)
positive.bed	Data frame, bed-formatted TRE loci.
negative.bed	Data frame, bed-formatted background loci.
file.prefix	String, the prefix for outputted BED file, no bed files output if NA
usecluster	Clustering matrix with 2 columns, 1st column is the index of motifs and 2nd column is the group number of clustering. It can be obtained from tfbs.clusterMotifs. If no clustering matrix, all motifs are used to do the comparson. see *details*
ncores	Number, comupting nodes in parallel environment.(default=3)
gc.correction	Logical value, if the difference between positive and negative TREs is significant,the resampling will be applied to the correction for the negative TREs. (default=FALSE)
fdr	Numeric value between 0 and 1, False Discovery Rate (FDR) of possible binding sites in rtfbs package, only binding sites with FDR less than this value can be selected.(default=0.1)
threshold	Numeric value, only sites with scores above this threshold are returned, not be used if NA. (default = NA)
gc.groups	Numeric value,indicating number of quantiles to group sequences into in rtfbs package. (default = 4)
background.order	Number, order of Markov model to build background.(default=2).
background.length	Number, length of the sequence to simulate background.(default=100000).
pv.adj	String, P-values correct method for p.adjust function. The available values are "holm", "hochberg", "hommel", "bonferroni", "BH", "BY","fdr" or "none". (default="bonferroni").

Details

The difference of GC contents between positive.bed and negative.bed is checked before the comparson. The p-value of Wilcox test and a vioplot figure show this difference and help the user to determine whether the correction is necessary. If the difference is very significant, please set *background.correction* to do background correction by resampling the TREs from negative bed data based on the frequency of TREs in negative bed data.

The clustering matix indicates which motifs in the 1st column are slected to do comparson and which clustering group in the 2nd columns are applied to adjust p-values for multiple comparsons. The function applys the p-values adjust for each clustering group. If no clustering information, all motifs in the tfbs object will be selected and adjusted as one group, which is the most conservative method.

Value

A object with the class name of "tfbs.comparson" will be resturned in this comparson function. It includes one list of parameters `parm` and one data frame of results `result`.

`result` is a data frame with the following columns:

`motif.id`	Motif ID.
`tf.name`	TF name.
`Npos`	TF site count found in positive ranges.
`Nneg`	TF site count found in negative ranges.
`es.ratio`	Enrichment score.
`pvalue`	p-value calculated by fisher test.
`pv.adj`	p-value corrected by the multiple correction.
`starch`	Binary filename of detected TF sites.

The `result` can be outputted to a report by the function `tfbs.reportComparson`.

See Also

`print.tfbs.comparson`, `summary.tfbs.comparson`, `tfbs.reportComparson`.

Examples

```
library(rtfbsdb);

file.twoBit     <- "/local/storage/data/hg19/hg19.2bit"

db <- CisBP.extdata("Homo_sapiens");
tfs <- tfbs.createFromCisBP(db, family_name="AP-2");


#make two dummy BED data frame for positive loci and negative loci
pos.bed <- data.frame(chr="chr1",
start=round(runif(100,1000000, 2000000)),
stop=0,
name="",
score=0,
strand=".");
pos.bed$stop <- pos.bed$start + 3000;

neg.bed <- data.frame(chr="chr1",
start=round(runif(200, 800000, 1800000)),
stop=0,
name="",
score=0,
strand=".");
neg.bed$stop <- neg.bed$start + round(runif(200, 1000, 3000));

t1 <- tfbs.compareTFsite( tfs,
      file.twoBit,
      pos.bed,
      neg.bed,
```

```
      gc.correction=TRUE,
      ncores = 1); #ncores=3

#Show a brief result
t1;

#Show the comparson results of all motifs
show(t1$result);

#Output the result to one pdf report.
tfbs.reportComparson(tfs, t1, file.pdf="test-tfbs-comp.pdf", sig.only=FALSE);
```

`tfbs.createFromCisBP` *Create TF object by querying the CisBP dataset.*

Description

Build a tfbs object by querying the meta file of CisBP dataset and subsetting the results.

Usage

```
tfbs.createFromCisBP(cisbp.db,
      tf_name = NULL,
      tf_status = NULL,
      family_name = NULL,
      motif_type = NULL,
      msource_id = NULL,
      tf.information.type = 1,
      expressed.only=TRUE,
      include.DBID.Missing=TRUE,
      seq.datatype=NA,
      file.bigwig.plus=NA,
      file.bigwig.minus=NA,
      file.bam=NA,
      file.twoBit=NA,
      file.gencode.gtf=NA,
      ncores = 1 )
```

Arguments

`cisbp.db`	A CisBP object("`CisBP.db`"), including the file of TF_Information.txt.
`tf_name`	String, indicating the TF_name field will be used to select motifs.
`tf_status`	String, indicating the TF_Status field will be used to select motifs.
`family_name`	String, indicating the Family_Name field will be used to select motifs.
`motif_type`	String, indicating the Motif_Type field will be used to select motifs.
`msource_id`	String, indicating the MSource_Identifier field will be used to select motifs.

`tf.information.type`
: Number,indicating which TF meta file will be used. Available values are 1 for TF_Information.txt, 2 for TF_Information_all_motifs.txt and 3 for TF_Information_all_motifs_plus.txt.

`expressed.only`
: Logical, indicating the only expressed TFs are selected to construct this object based on the gene exprssion values.

`include.DBID.Missing`
: Logical, indicating whether the TFs without association with GENCODE through the DBID are selected.

`seq.datatype`
: String,indicating which kind of seq data is applied to this function, three values are available: GRO-seq, PRO-seq and RNA-seq. Default: GRO-seq

`file.bigwig.plus`
: String, indicating bigwig file for strand plus(+) if `seq.datatype` is GRO-seq or PRO-seq.

`file.bigwig.minus`
: String, indicating bigwig file for strand minus(-) if `seq.datatype` is GRO-seq or PRO-seq.

`file.bam`
: String, indicating BAM file for rna reads if `seq.datatype` is RNA-seq.

`file.twoBit`
: String, indicating the binary data of sequence. (e.g. hg19.2bit, mm10.2bit)

`file.gencode.gtf`
: String,indicating Gencode GTF file downloaded from the Gencode web site.

`ncores`
: Number, comuputing nodes in parallel environment for gencode data converting.

Details

The function includes three steps to build a tfbs object:
1) Searching the TF information and PWM files in the CisBP dataset according to the criteria specified by the parameters of *tf_name*, *tf_status*, *family_name*, *motif_type* and *msource_id*.
2) If `seq.datatype` is GRO-seq or PRO-seq and the bigwig files are provided, the gene expression values are calculated through querying the TREs region from the GENCODE database(for human, gencode.v21.annotation.gtf, for mouse: gencode.vM3.annotation.gtf)
and querying the reads count in the plus and minus bigWig files.

If `seq.datatype` is RNA-seq and the BAM file is provided, read counts for each TRE regions will be queried from the BAM file.

3) If the expressed TFs only is used in the tfbs object, the TFs with p-values corrected by Bonfrroni less than 0.05 will be selected.

The following part explains how to calculate the gene expression.

For each motif, the occurance ranges can be queried by the gene ID After the searching, one range obtained from the merge of the multiple ranges will be used to detect the reads count in the specified bigwig files(including plus and minus). The probability of each motif can be calcuated by the reads count and lambda.

The lambda is determined by the following formulation:

```
r.lambda = 0.04 * sum(reads_in_all_chromosomes)/10751533/1000.
```

The dataset of GENECODE v21 (human) and vM3 (mouse) have been compiled into RDATA file and attached in this package.

The `gencode_transcript_ext` object can be accessed after the following command is executed successfully.

```
load( system.file("extdata", "gencode_v21_transcript_ext.rdata",      package="r
```

Value

A tfbs object is returned with PWM matrices, see Also as "`tfbs`"

See Also

See Also as `tfbs`

Examples

```
# Load the internal CisBP dataset
db_human <- CisBP.extdata("Homo_sapiens");

# Load all motifs and return a tfbs object.
tfs0 <- tfbs.createFromCisBP(db_human);

# Query the motifs by the conditions and return a tfbs object
tfs1 <- tfbs.createFromCisBP(db_human, family_name="Homeodomain", tf_status="D",
      motif_type="ChIP-seq", msource_id= "MS01_1.01", tf.information.type=1 );

# Query the motifs by the conditions and return a tfbs object
tfs2 <- tfbs.createFromCisBP(db_human, family_name="Homeodomain", tf_status="D" );

# Query the motifs by the conditions and return a tfbs object
tfs3 <- tfbs.createFromCisBP(db_human, motif_type="ChIP-seq"  );

# Query the motifs by the conditions and return a tfbs object
tfs4 <- tfbs.createFromCisBP(db_human, tf.information.type=2);
```

---

tfbs.db-class *Class* "tfbs.db"

Description

Abstract class for motif dataset. The CisBP class is a son class of tfbs.db.

Objects from the Class

Now code or function can be used to create this class.

Slots

`species`: Species name.

Methods

No methods defined with class "tfbs.db" in the signature.

See Also

"`CisBP.db`" inherits this class.

Examples

```
showClass("tfbs.db")
```

`tfbs.dirs` *Create a tfbs object from the folders.*

Description

Create a tfbs object from all the PWM files found in the supplied folders.

Usage

```
tfbs.dirs(...,
      species = "Homo_sapiens",
      args.read.motif = NULL,
      pattern = glob2rx("*.pwm"),
      recursive = FALSE)
```

Arguments

`...`	Multiple strings, one or more folders can be used in this function.
`species`	String, including the species name.
`args.read.motif`	List, including *pseudocount*, *force_even* or other parameters used in `read.table` function.
`pattern`	String, a character vector specifying regular expression and wlidcards.
`recursive`	Logical, indicating the loading recursively descends into subfolders or not, default: FALSE.

Details

Two parameters in the list of `args.read.motif` can be used:
pseudocount: log value for zero value in PWM matrix, default is -7.
force_even: whether the PWM matrix with odd size needs to be even.

Value

A tfbs object collecting all the PWM files in the specified folders. For the details of tfbs object, please see tfbs

See Also

The structure of tfbs object is described in "tfbs"

Examples

```
fs.dir <- system.file("extdata","", package="rtfbsdb")
tfs <- tfbs.dirs( fs.dir,
      args.read.motif = list(pseudocount=-7, header=TRUE, sep="\t" , row.names=1) );
str(tfs);
```

---

tfbs.drawLogo *Draw single motif logo.*

Description

Draw the motif logos in two models, 1 logo within a page or 1 group within one page.

Usage

```
tfbs.drawLogo(tfbs, file.pdf = NULL, index = NULL, tf_id = NULL,
                motif_id = NULL, tf_name = NULL, family_name = NULL,
                tf_status = NULL, groupby = NULL)
```

Arguments

tfbs	A tfbs object("tfbs")
file.pdf	String, the file name of PDF report.
index	Vector of number, indicating the motif index.
tf_id	Vector of string, indicating the TF_ID string, TF_ID is one motif attribute in TF_Information.txt. (Default=NULL).
motif_id	Vector of string, indicating the Motif_ID string, Motif_ID is one motif attribute in TF_Information.txt. (Default=NULL).
tf_name	Vector of string, indicating the TF_Name string, TF_Name is one motif attribute in TF_Information.txt. (Default=NULL).
family_name	Vector of string, indicating Family_Name string, Family_Name is one motif attribute in TF_Information.txt. (Default=NULL).
tf_status	String, indicating the TF_status value, TF_status is one motif attribute in TF_Information.txt. (Default=NULL).
groupby	String, indicating the group field is applied to print the motif, each group is printed in one page, the available values are NA, "Family_Name", "TF_Name", "TF_Status" or "Motif_Type". (Default=NA).

Details

Multiple selection is provided for outputting logos. The selected motifs by each criteria will be combined into one set.

Draw the motif logos in two models:
(1) 1 logo within a page (2) 1 group within one page.The motif logos are splitted if motif count is greater than 10.

Value

No return values.

See Also

See Also as "tfbs"

Examples

```
db <- CisBP.extdata("Homo_sapiens");

tfs <- tfbs.createFromCisBP(db);

motif_id   <- c( "M5604_1.01", "M5441_1.01", "M5162_1.01", "M5352_1.01");
tf_id      <- c( "T093250_1.01", "T093251_1.01","T093252_1.01","T093253_1.01");
family_name<- c( "p53", "Homeodomain", "Paired box", "Pipsqueak");


#Draw 10 motif logos from first one.
tfbs.drawLogo(tfs, file.pdf="tfbs.drawLogo1.pdf", index=c(1:10) );

#Draw logos for specified Motif_ID, or TF_ID, or TF_Name, or Family_Name
tfbs.drawLogo(tfs, file.pdf="tfbs.drawLogo2.pdf",
 motif_id=motif_id,
 tf_id=tf_id,
 tf_name="AP-2",
 family_name=family_name,
 groupby="TF_Status");

#Draw logos for specified TF_Status
tfbs.drawLogo(tfs, file.pdf="tfbs.drawLogo3.pdf", tf_status="D", groupby="TF_Status");

#unlink("tfbs.drawLogo1.pdf");
#unlink("tfbs.drawLogo2.pdf");
#unlink("tfbs.drawLogo3.pdf");
```

---

tfbs.drawLogosForClusters

Draw the motif logos by clustering.

Description

Draw the motif logos by one cluster per page.

Usage

```
tfbs.drawLogosForClusters(tfbs, cluster.mat, file.pdf )
```

Arguments

tfbs	A tfbs object("tfbs").
cluster.mat	A matrix with 2 columns returned by tfbs.clusterMotifs, 1st column is the index of motifs and 2nd column is the group number of clustering.
file.pdf	String indicating a PDF eilname.

Details

It is different with tfbs.drawLogo which is capable of printing out motif logos in group. This group is calculated by the tfbs.clusterMotifs, not is classfied by any group filed.

Value

No return value.

See Also

See Also as tfbs.clusterMotifs

Examples

```
# Load the internal CisBP data set
db <- CisBP.extdata("Homo_sapiens");

# Create a tfbs object by querying the meta file of CisBP dataset.
tfs <- tfbs.createFromCisBP(db, motif_type="ChIP-seq", tf.information.type=1 );

# Calculate the distance matrix
tfs <- tfbs.getDistanceMatrix( tfs, ncores=1);

# Cluster the motifs using the "cors" method
cluster1 <- tfbs.clusterMotifs(tfs, pdf.heatmap = "test-heatmap1.pdf", method="cors" );
show(cluster1);

# draw motif logos on one group per page.
tfbs.drawLogosForClusters(tfs, cluster1, "test-cluster1.pdf")
```

`tfbs.getDistanceMatrix` *Calcuate a distance matrix with Pearson's R values.*

Description

Compare any two motifs and return a matrix with Pearson's R values.

Usage

```
tfbs.getDistanceMatrix(tfbs, ncores = 3, BG = log(c(0.25, 0.25, 0.25, 0.25)))
```

Arguments

`tfbs`	A tfbs object("tfbs").
`ncores`	Number, the number of cores to use simultaneously.
`BG`	The log value of probabilities for nucleotide A, C, G and T as Backgroud computing.

Details

Please do it parallel computation if you can use multi-cores because the calculation takes long time.

Value

A tfbs object with new distance matrix (@distancematrix).

See Also

"tfbs"

Examples

```
db <- CisBP.extdata("Homo_sapiens");
tfs <- tfbs.createFromCisBP(db, family_name="AP-2");
tfs0 <- tfbs.getDistanceMatrix(tfs, ncores=1);
```

`tfbs.getExpression` *Estimate gene expression of target TF.*

Description

Gets expression level of target TF.
USE extra_info$DBID to find gene information encoded by GENCODE V21

Usage

```
tfbs.getExpression(tfbs,
      file.bigwig.plus, file.bigwig.minus,
      file.bam=NA,
      file.twoBit=NA,
      file.gencode.gtf=NA,
      seq.datatype=NA,
      ncores =3 )
```

Arguments

tfbs	A tfbs object("tfbs").
file.bigwig.plus	String, indicating bigwig file for strand plus(+) if seq.datatype is GRO-seq or PRO-seq.
file.bigwig.minus	String, indicating bigwig file for strand minus(-) if seq.datatype is GRO-seq or PRO-seq.
file.bam	String, indicating BAM file for rna reads if seq.datatype is RNA-seq.
file.twoBit	String, indicating the binary data of sequence. (e.g. hg19.2bit, mm10.2bit)
file.gencode.gtf	Gencode RDATA file encoded by ths package.
seq.datatype	String,indicating which kind of seq data is applied to this function, three values are available: GRO-seq, PRO-seq and RNA-seq. (Default=GRO-seq)
ncores	Number, comupting nodes in parallel environment.

Details

For each motif, the occurance ranges can be queried by the gene ID in the GENCODE database(for human, gencode.v21.annotation.gtf, for mouse: gencode.vM3.annotation.gtf). After the searching, one range obtianed from the merge of the multiple ranges will be used to detect the reads count in the specified bigwig files(including plus and minus). The probability of each motif can be calcuated by the reads count and lambda.

The lambda is determined by the following formulation:

```
r.lambda = 0.04 * sum(reads_in_all_chromosomes)/10751533/1000.
```

The dataset of GENECODE v21 (human) and vM3 (mouse) have been compiled into RDATA file and attached in this package.

The gencode_transcript_ext object can be accessed after the following command is executed successfully.

```
load( system.file("extdata", "gencode_human21_transcript_ext.rdata",      packag
```

Value

A tbfs object with new expression data frame including the follwing columns:

`Motif_ID`	Motif_ID from CisBP dataset or other data source.
`DBID`	DBID from CisBP dataset or other data source.
`chr`	String, chromosome name.
`start`	Integer, start postion in which gene ID can be detected.
`end`	Integer, end postion in which gene ID can be detected.
`strand`	String, + or -, indicating the strand direction.
`bed_length`	Integer, the length of range which gene ID can be detected.
`reads`	The reads number queried by BigWig function from the bigwig files(plus and minus)
`lambda`	The lambda parameter in poison distribution.
`prob`	The probability calculated based on Poisson distribution.

See Also

See Also as "`tfbs`"

Examples

```
# Load the internal CisBP data set
db.human <- CisBP.extdata("Homo_sapiens");

# Create a tfbs object by querying the meta file of CisBP dataset.
tfs <- tfbs.createFromCisBP(db.human, motif_type="ChIP-seq", tf.information.type=1 );

if(0)
{
file.bigwig.plus <- "testdata//GSM1480327_K562_PROseq_plus.bw";
file.bigwig.minus <-"testdata/GSM1480327_K562_PROseq_minus.bw";

tfs <- tfbs.getExpression(tfs, file.bigwig.plus, file.bigwig.minus,
       file.gencode.gtf="/local/storage/data/gencode/gencode.v21.annotation.gtf" );

tfs <- tfbs.getExpression(tfs, file.bigwig.plus, file.bigwig.minus, ncores = 21 );
}
```

`tfbs.reportComparson`

Output report for comparson results.

Description

Output comparson results to a PDF report which includes motif names, counts of TF site, p-value, enrichment ratio and motif logos.

Usage

```
tfbs.reportComparson(tfbs, r.comp,
      file.pdf = NA,
      report.size = "letter",
      report.title = "",
      sig.only = TRUE,
      pv.cutoff = 0.05,
      pv.adj = NA)
```

Arguments

tfbs	A tfbs object, see also "tfbs"
r.comp	A result object from the function of tfbs.compareTFsite
file.pdf	String, the file name of PDF report.
report.size	String, the page size (default="letter")
report.title	String, the report title.
sig.only	String, indicating whether only significant motifs are outputted or not.(default=TRUE).
pv.cutoff	Numeric value,indicating whether the different cutoff of p-value is applied to select the significant motifs.
pv.adj	String,indicating whether the different correction metod of p-value is applied to select the significant motifs.

Details

The table with 7 columns is outputted into a PDF report within letter size.
Two color bars are used to display p-values and enrichment ratios. Motif logos are shown visually in each row.

Value

No return values.

See Also

tfbs.compareTFsite, summary.tfbs.comparson.

Examples

```
# see examples in tfbs.compareTFsite
```

`tfbs.reportFinding` *Make report for scanning results.*

Description

Output a PDF report includes motif names, counts of TF site and motif logos.

Usage

```
tfbs.reportFinding(tfbs,
      r.scan,
      file.pdf = NA,
      report.size = "letter",
      report.title = "")
```

Arguments

`tfbs`	A tfbs object, see also "`tfbs`"
`r.scan`	A result object from the function of `tfbs.scanTFsite`
`file.pdf`	String, the file name of PDF report.
`report.size`	String, the page size (default="letter")
`report.title`	String, the report title.

Details

The table with 4 columns is outputted into a PDF report within letter size.
Motif logos are shown visually in each row.

Value

No return values.

See Also

`tfbs.scanTFsite`, `print.tfbs.finding`

Examples

```
#See example in tfbs.scanTFsite
```

`tfbs.scanTFsite` *Find TF sites from genome data within the BED loci*

Description

Find TF sites from genome data within the BED loci. Please notice that this package does not provided genome data such as hg19.2bit, mm10.2bit.

Usage

```
tfbs.scanTFsite(tfbs,
      file.twoBit,
      tre.bed,
      return.type=c("matches", "posteriors", "maxposterior", "writedb"),
      file.prefix=NA,
      usemotifs = NA,
      ncores = 3,
      fdr = NA,
      threshold = 6,
      gc.groups = NA,
      background.order = 2,
      background.length = 100000)
```

Arguments

`tfbs`	A tfbs object (`"tfbs"`) returned by `tfbs.createFromCisBP`, `tfbs`, `tfbs.dirs`.
`file.twoBit`	String, the file name of genome data(e.g. hg19.2bit or mm10.2bit)
`tre.bed`	Data frame, bed-formatted loci information with 6 columns
`return.type`	String, four available values explained in th details(default = "matches")
`file.prefix`	String, the prefix for outputted file, only used when the return.type is *writedb*
`usemotifs`	Vector indicating indexes of motif to be used in scanning.
`ncores`	Number, computing nodes in parallel environment (default = 3).
`fdr`	Numeric value between 0 and 1, False Discovery Rate (FDR) of possible binding sites in `rtfbs` package, only binding sites with FDR less than this value can be selected. If fdr value is assigned, the `threshold` will be ignored.
`threshold`	Numeric value, only sites with scores above this threshold are returned in `rtfbs` package (default = 6).
`gc.groups`	Numeric value,indicating number of quantiles to group sequences into in `rtfbs` package (default = 1).
`background.order`	Numeric value,indicating the order of Markov model to build in `rtfbs` package (default = 2).
`background.length`	Numeric value, indicating length of the sequence to simulate in `rtfbs` package (default = 100000)

Details

(1) Four options are availabe for the function of tfbs.scanTFsite as follows.

- matches: returns all matching TF sites for all motifs.
- writedb: writes a bed file with matches sites. Assumes that sort-bed and starch tools are availiable in $PATH
- posteriors: returns the posteriors at each position in bed-formatted loci.
- maxposterior: returns the max(posterior) in each position in bed-formatted loci.

(2) In order to make the binary file with the parameter of writedb, make sure that starchcat and sort-bed command (in BEDOPS) can be accessed from R environment. If not, please put the folder in $PATH.

Value

A list object will be returned with the class name of `tfbs.finding`. The object wraps four sub-list as follows:

1) `parm`:Calling parameters(`fdr`, `threshold`), `gc.groups`...).
2) `bed`: Calling bed-formatted loci(`tre.bed`).
3) `summary`: A data frame including summrized information about matched TF sites for all motifs.
4) `result`: Scanning results which data type is depend on the parameter of `return.type`.

The option of *matches* returns a list including the result of every motif, which result is BED style data frame with the following columns.

`chrom`	chromosome
`chromStart`	start position
`chromEnd`	chromosome end position
`name`	
`score`	The score is given by the log likelihood ratio against the Marklov model(backgound).
`strand`	strand

The option of *writedb* will return a binary BED filename in which store all bed ranges.

The option of *posteriors* will return a list for each motif returned by score.ms function. Scores represent the motif 'match score', or the product of the probability of observing each base under the motif or background models. Scores are returned under the motif model for all positions in the sequence, on both forward and reverse strands, and under the background model.

The option of *maxposterior* will return a probability matrix which the row indicates the target loci and the column indicates the motif.

See Also

`print.tfbs.finding`, `summary.tfbs.finding`, `tfbs.reportFinding`.

Examples

```
library(rtfbsdb);
file.twoBit     <- "/local/storage/data/hg19/hg19.2bit"

db <- CisBP.extdata("Homo_sapiens");
tfs <- tfbs.createFromCisBP(db, family_name="AP-2");

tre.bed <- data.frame(chr="chr1",
start=round(runif(10,1000000, 2000000)),
stop=0,
name="",
score=0,
strand=".");
tre.bed$stop <- tre.bed$start + 3000;

t1 <- tfbs.scanTFsite( tfs,
file.twoBit,
tre.bed,
file.prefix="test.db",
ncores = 1);

#show a brief information about the result
t1

#show the summary information in the result
show(t1$summary);

#show the matched TF sites for first motif
show(t1$result[[1]]);

#Output a PDF report for all motifs.
tfbs.reportFinding(tfs, t1, file.pdf="Test Results");

t2 <- tfbs.scanTFsite( tfs,
file.twoBit,
tre.bed,
file.prefix="test.db",
return.type="writedb",
ncores = 1);

t2

t3 <- tfbs.scanTFsite( tfs,
file.twoBit,
tre.bed,
return.type="posteriors",
ncores = 1);

t3

t4 <- tfbs.scanTFsite( tfs,
file.twoBit,
tre.bed,
return.type="maxposterior",
ncores = 1);
```

```
t4;

t4$result;
```

`tfbs.selectByGeneExp` *Motif selection by gene expression level.*

Description

Select the motifs with minimum p-value from each group of clustering.

Usage

```
tfbs.selectByGeneExp(tfbs, cluster.mat)
```

Arguments

`tfbs`	A tfbs object ("`tfbs`") with the data frame of gene expression level.
`cluster.mat`	A matrix with 2 columns returned by `tfbs.clusterMotifs`, 1st column is the index of motifs and 2nd column is the group number of clustering.

Details

The function of `tfbs.getExpression` should be successfully called and the results of gene expression should be returned before this function is called. The indexes of selected motifs will be used in the function of `tfbs.compareTFsite` or `tfbs.scanTFsite`.

Value

A vector of motif indices is returned.

See Also

See Also as `tfbs.selectByRandom`, `tfbs.getExpression`

Examples

```
db <- CisBP.extdata("Homo_sapiens");

tfs <- tfbs.createFromCisBP(db, family_name="AP-2");

if(0)
{
tfs <- tfbs.getExpression(tfs, file.bigwig.plus, file.bigwig.minus, file.hg19);

cluster1 <- tfbs.clusterMotifs(tfs, pdf.heatmap="test-AP2-heatmap.pdf" );

usemotif <- tfbs.selectByGeneExp(tf, cluster1);
}
```

`tfbs.selectByRandom` *Random motif selection*

Description

Select the motifs randomly from each group of clustering.

Usage

```
tfbs.selectByRandom(tfbs, cluster.mat)
```

Arguments

`tfbs`	A tfbs object("`tfbs`").
`cluster.mat`	A matrix with 2 columns returned by `tfbs.clusterMotifs`, 1st column is the index of motifs and 2nd column is the group number of clustering.

Details

The indexes of selected motifs can be used in the function of `tfbs.compareTFsite` or `tfbs.scanTFsite`.

Value

A vector of motif indices is returned.

See Also

See Also as `tfbs.selectByGeneExp`, `tfbs.getExpression`

Examples

```
db <- CisBP.extdata("Homo_sapiens");

tfs <- tfbs.createFromCisBP(db, family_name="AP-2");

tfs <- tfbs.getDistanceMatrix(tfs, ncores=1);

cluster1 <- tfbs.clusterMotifs(tfs, pdf.heatmap="test-AP2-heatmap.pdf" );

usemotif <- tfbs.selectByRandom(tfs, cluster1);

show(usemotif);
```

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